THE ATHENA AGENDA

ADVANCING THE APOLLO PROGRAM FOR BIODEFENSE

A REPORT BY THE
BIPARTISAN COMMISSION ON BIODEFENSE

April 2022

BIPARTISAN COMMISSION ON BIODEFENSE

THE ATHENA AGENDA

ADVANCING THE APOLLO PROGRAM FOR BIODEFENSE

A REPORT BY THE
BIPARTISAN COMMISSION ON BIODEFENSE

April 2022

BIPARTISAN
COMMISSION
ON BIODEFENSE

www.biodefensecommission.org

Graphics and design by Factor3 Digital,
Base cover art by Shutterstock.

SUGGESTED CITATION

Bipartisan Commission on Biodefense. (2022).
The Athena Agenda: Advancing The Apollo Program for Biodefense.
Bipartisan Commission on Biodefense: Washington, D.C.

COMMISSIONERS

Joseph I. Lieberman, Chair

Thomas J. Ridge, Chair

Donna E. Shalala

Thomas A. Daschle

Susan W. Brooks

James C. Greenwood

Margaret A. Hamburg

Kenneth L. Wainstein

EX OFFICIO MEMBERS

Yonah Alexander, PhD

William B. Karesh, DVM

Rachel Levinson, MA

I. Lewis Libby, JD

Gerald W. Parker, DVM, PhD

George Poste, DVM, PhD, DSc

Tevi Troy, PhD

STAFF

Asha M. George, DrPH, Executive Director

Ambika Bumb, PhD, Deputy Executive Director

Robert H. Bradley, Policy Principal

John T. O'Brien, MS, Research Associate

Arienne O'Neil, Office Manager

Patricia de la Sota, Event Coordinator

ACKNOWLEDGMENTS

We thank the scientists, technologists, and policy experts who support and provided their input on The Apollo Program for Biodefense and The Athena Agenda. We commend Dr. Jacob Swett for his leadership and his tireless efforts to advance science, technology, and biodefense. We also thank Shelly Holland, Bill Beaver, Dr. Michelle Holko, Dr. Anastasia Lambrou, Andrew Bo Liu, Dr. Cassidy Nelson, Georgia Ray, and Dr. Brian Wang for their efforts to seek out the information and expertise we needed to inform the initial Apollo Program for Biodefense report. We also thank Dr. David J. Ecker and Dr. Jassi Pannu for their advice and input on The Apollo Program for Biodefense and The Athena Agenda, in addition to Justin M. Chan for his contributions in providing historical context for both reports. The Commission extends its gratitude to Dr. Gregory Koblentz and Dr. Stephen Hahn for their advice on The Athena Agenda recommendations. We gratefully acknowledge the advice of Dr. Jason Matheny and Dr. Tara O'Toole with regard to the continuous pursuit of this Program. We thank Dr. Tevi Troy, Dr. George Poste, and Rachel Levinson for their good counsel, as well as the review and comments provided by the Commission's other ex officio members. Additionally, we greatly appreciate the support of our donors, and that of Hudson Institute, which serves as our fiscal sponsor.

TABLE OF CONTENTS

PREFACE

On September 12, 1962, President John F. Kennedy spoke to the nation and said those immortal words, "We choose to go to the Moon in this decade and do the other things — not because they are easy but because they are hard."

These words could have been written off as an impossible challenge doomed to fail. Instead, it galvanized the country and brought us together for the benefit of all humankind.

Today, we are faced with our own seemingly impossible challenge: we must stop pandemics before they can ever take hold again. And just like the race to the Moon, it will take our best and brightest to reach our final destination. But most importantly, it will take all of us coming together once again for the common good.

Each of us is experiencing firsthand the devastating effects of pandemics. It is becoming painfully obvious that we must put an end to this threat and prevent them once and for all.

Despite all the turmoil and grief of the past two years, there is hope. We developed a vaccine in less than a year, pushing technology and innovation beyond what was thought possible, and we created new treatments and diagnostics. Yet, while we stemmed the tide and averted an even greater catastrophe, we might not be so lucky next time. Whether natural, accidental, or deliberate, infectious disease threats are increasing in frequency and severity. It is a question of when, not if, the next pandemic arrives.

It is for this very reason that we must act now. Fortunately, there are those who have already answered the call and joined forces to advocate for an Apollo Program for Biodefense. Our nation has a history of accomplishing remarkable things when we put our minds to it. From a system of highways that connected the country to a global positioning system that helps us find our way, our country has always been able to achieve what has never been done before, particularly when we take on technological challenges.

But this challenge will take sustained bipartisan support and stalwart leadership. Both public and private sectors must work together, with the private sector providing expertise and capital to support research, clinical trials, regulatory expertise, and manufacturing

scale, while government supports fundamental research and incentives for innovation. And since this problem is a threat to all, we must work with other countries in a US-led initiative, strengthening our international relationships and harnessing other countries and international stakeholders as our partners in this fight.

The Apollo Program for Biodefense will not focus on a singular track, but rather involve the pursuit of multiple, parallel, groundbreaking solutions that together will end the frequency and severity of these emerging threats. We will create a world where we can detect new pathogens and continually trace them from the source, and where we can distribute rapid point-of-use tests to every household in the country within days of detection. Instant capture of test data will generate real-time situational awareness to optimize decisions so that already-in-hand treatments can be effectively and efficiently rolled-out.

While we achieve these goals, we will advance other areas of knowledge across the whole spectrum of science, technology, engineering, and mathematics. These advancements will inspire scientists, physicians, healthcare personnel, engineers, and data scientists to operate in an integrated innovation ecosystem that encourages high risk, high reward research. They will also support entrepreneurial investment within agile regulatory frameworks and public policies to adapt to the growing complexity of the threat spectrum.

Living through this pandemic created momentum to produce technologies and solutions that we previously lacked the will or resources to pursue. We must build on that progress and push for greater advances that will protect us from the next infectious disease threat.

We envision a time when people will look back and wonder how we ever let infectious diseases wreak havoc on our society—how we ever tolerated seasonal flu, let alone viruses like COVID-19.

This noble and extraordinary mission can be fully realized by the end of this decade. However, this will require visionary leadership and a commitment to implement intellectual, financial, and infrastructure investments, along with purposeful and proactive construction of relevant public-private partnerships. Success will also depend on forceful actions to transcend current institutional silos and technical constraints, while also avoiding the historical cycles of crisis and ‘out of sight, out of mind’ policies. The time is now.

"The Apollo Program for Biodefense will not focus on a singular track, but rather involve the pursuit of multiple, parallel, groundbreaking solutions that together will end the frequency and severity of these emerging threats.

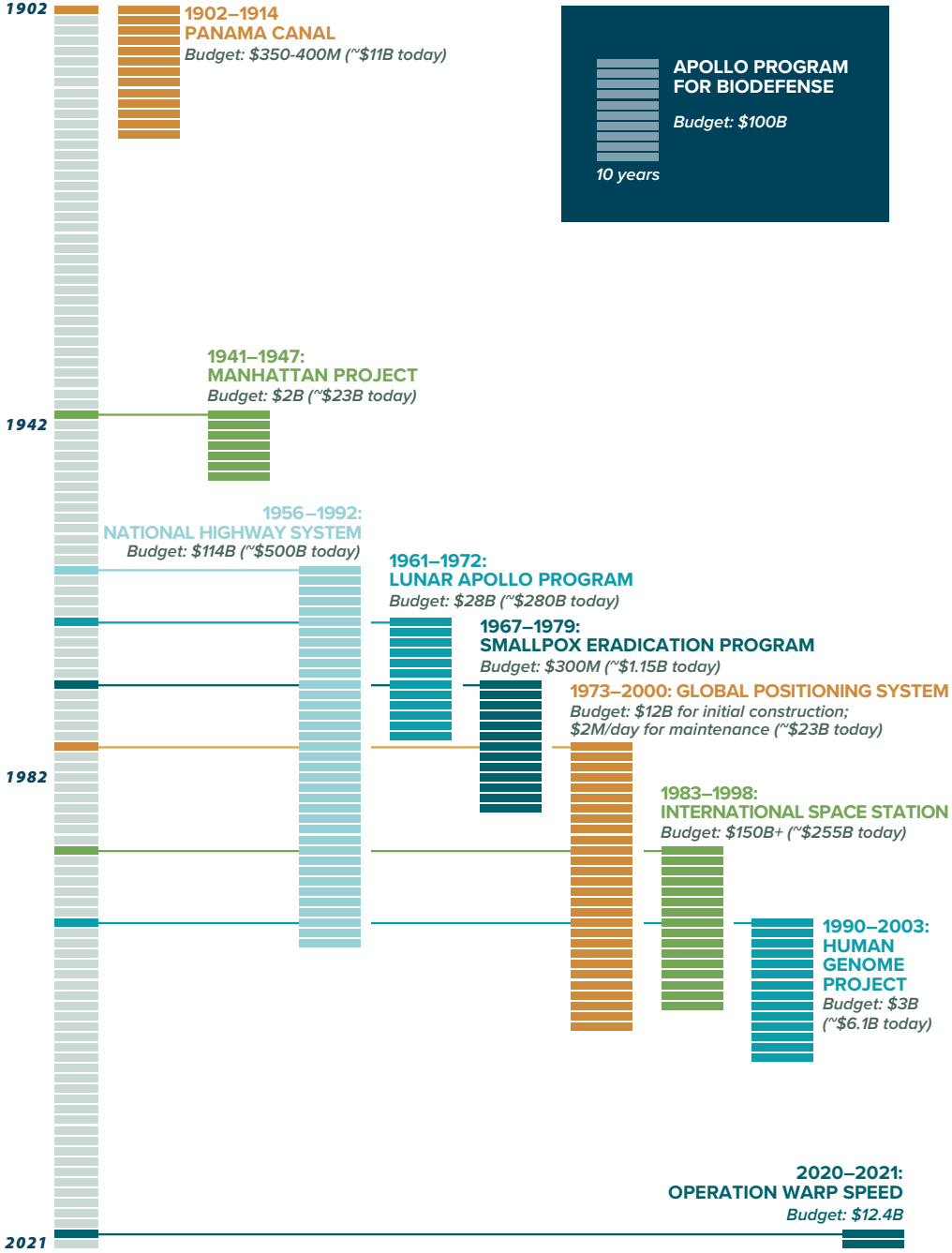
EXECUTIVE SUMMARY

The Bipartisan Commission on Biodefense warned that the United States was woefully unprepared for biological threats and that the risk to the Nation was rising rapidly in our baseline 2015 report, *A National Blueprint for Biodefense: Leadership and Major Reform Needed to Optimize Efforts.*[1] A little over six years later, the US experience with COVID-19 and the proliferation of biological weapons programs[2] continue to validate our original findings.

Since we released *The Apollo Program for Biodefense: Winning the Race Against Biological Threats* in January 2021, the world has yet to surmount COVID-19. Nearly one million American deaths and more than $16 trillion[3] in US economic losses have made COVID-19 the deadliest pandemic in this country's history and the costliest domestic catastrophe since the Great Depression. This pandemic has killed over six million people around the world,[4] ravaged health systems,[5] destroyed economies,[6] and exposed destabilizing divisions within[7] and among countries.[8] And yet, the Commission remains convinced that COVID-19 is not a once-in-a-century pandemic. Another biological event will occur much earlier than that.[9]

The risk of naturally occurring pandemics grows as biodiversity is reducing due to deforestation and diminished wildlife habitat quality. The exploitation of wildlife through hunting and trade facilitates opportunities for animal–human interactions and zoonotic disease transmission. Furthermore, advances in DNA sequencing, gene-editing, and synthetic biology (among others) hold the promise of profound advances in healthcare, crop and environmental sustainability, and economic growth. Unfortunately, these are dual-use technologies that could yield accidental, unintended, and deliberate misuse by creating deadly pathogens or disrupting ecological balances. Examples include the accidental release of smallpox from a laboratory in the United Kingdom,[10] engineering of a deadly strain of influenza by a professor in the Netherlands,[11] inadvertent self-injection of Ebola by an experienced scientist in Russia,[12] and the unintended escape of Brucellosis from an industrial facility in China.[13]

Figure 1. United States Grand Programs.



Our country must decide to make the prevention and deterrence of the next biological incident top priorities. We cannot simply afford to focus on the response to the current pandemic, but must work to put in place mitigation measures to reduce the impact of future biological events. Continuing vulnerabilities revealed by biological threats increase the likelihood that our enemies will attack our country with biological weapons,[14] especially as advances in science and technology make it easier to produce such weapons.

Throughout our country's history, our government has risen to seemingly impossible challenges by pursuing grand programs. It was hard to imagine landing a person on the Moon in 1961 when President John F. Kennedy committed the United States to achieving that goal in 10 years. Our country accomplished the Apollo 11 mission 9 years later, with 161 days to spare. The United States can similarly put an end to pandemics within a decade.

The Athena Agenda: Advancing The Apollo Program for Biodefense **contains additional recommendations to execute The Apollo Program, building on the Commission's previous work and taking into consideration the efforts of current and former Administrations and Congresses. This report provides the following specific governance and technology recommendations to implement The Apollo Program for Biodefense and identifies the US government organizations responsible for leadership and accountability, though certain actions may require or benefit from public-private partnerships.**

Figure 2. Recommendations in the Athena Agenda and their federal implementers.

ATHENA AGENDA RECOMMENDATIONS: GOVERNANCE

Fully Implement the National Blueprint for Biodefense
a. Prioritize innovation over incrementalism in medical countermeasure development
b. Fully prioritize, fund, and incentivize the medical countermeasure enterprise
c. Reform Biomedical Advanced Research and Development Authority contracting
d. Incentivize development of rapid point-of-care diagnostics
e. Develop a 21st Century-worthy environmental detection system
f. Review and overhaul the Select Agent Program
g. Lead the way towards establishing a functional and agile global public health response apparatus
Implementer: White House, Congress, Federal government

Implement The Apollo Program for Biodefense (or its equivalent)
a. Produce a National Biodefense Science and Technology Strategy
Implementer: White House (National Security Council (NSC)), Office of Science and Technology Policy (OSTP)
b. Implement The Apollo Program for Biodefense (or its equivalent)
Implementer: Congress, White House (NSC, OSTP, Office of Management and Budget (OMB), Department of State (DOS)), Department of Commerce (DOC), Department of Defense (DOD), Department of Education (ED), Department of Homeland Security (DHS), Department of Labor (DOL), Department of the Interior (DOI), Department of Transportation (DOT), Department of Health and Human Services (HHS), Department of Agriculture (USDA), Director of National Intelligence (DNI), Environmental Protection Agency, National Aeronautics and Space Agency (NASA), National Science Foundation (NSF)
c. Require a cross-cutting budget for The Apollo Program for Biodefense (or its equivalent)
Implementer: White House (OMB)

Provide appropriations to implement The Apollo Program for Biodefense (or its equivalent)
a. Appropriate funds for those federal departments and agencies contributing to The Apollo Program for Biodefense (or its equivalent).
Implementer: Congress
b. Provide multi-year budget authority
Implementer: Congress

Continued

Produce a comprehensive mid- and post-crisis report on continuity of government for COVID-19

Implementer: Congress, White House (NSC), Federal Emergency Management Agency (FEMA)

Revamp regulatory processes and policies to authorize or approve innovative technologies before, during, and after biological events

Implementer: Food and Drug Administration (FDA)/HHS

a. Modernize and accelerate approval pathways for platform technologies to produce medical countermeasures

Implementer: Congress, FDA/HHS

b. Incorporate lessons learned from COVID-19

Implementer: Congress, FDA/HHS

Develop a strategy and implementation plan for distributing at-home tests and therapeutics

Implementer: Congress, Assistant Secretary for Preparedness and Response (ASPR)/HHS, United States Postal Service

Support urgently needed public health measures for research during biological events

Implementer: Congress, National Institutes of Health (NIH)/HHS

Improve risk communications and build public trust

Implementer: Centers for Disease Control and Prevention (CDC)/HHS

a. Develop a strategy for crisis and risk communications that builds public trust

Implementer: White House, HHS, CDC/HHS

ATHENA AGENDA RECOMMENDATIONS: TECHNOLOGY

Develop at least one vaccine candidate for each of the 26 viral families that infect humans

Implementer: Congress, HHS, DOD, USDA

Develop a suite of broad-spectrum antiviral drugs.

Implementer: Congress, HHS, USDA, DOD

Develop a strategy for the rapid development of a virus-specific antiviral during an emerging outbreak.

Implementer: Congress, HHS

Review previous advanced manufacturing capability efforts for technologies for medical countermeasures

Implementer: Congress, DOD, HHS

Continued

Expand advanced manufacturing capability for platform technologies for medical countermeasures

Implementer: Congress, DOD, HHS

Produce a research and development plan for needle-free methods of drug and vaccine administration

Implementer: HHS, DOD, USDA

Increase US sequencing capability and capacity

Implementer: Congress, HHS, DOD, Department of Energy (DOE), USDA

Identify the need for portable sequencing capabilities

Implementer: HHS, DOD, USDA, DHS

Develop affordable portable sequencing

Implementer: HHS, DOD, USDA

Further develop the ability to detect infections with minimally- and non-invasive methods

Implementer: Congress, HHS, DOD, USDA

Advance massively multiplexed detection capabilities

Implementer: Congress, DOD, HHS, DHS

Invest in point-of-use diagnostics

Implementer: HHS, NIH/HHS

Develop a plan for rapid development, approval, scaling, acquisition, procurement, and distribution of point-of-use diagnostic tests

Implementer: HHS, NIH/HHS, DOD

Invest in digital pathogen surveillance

Implementer: Congress, HHS, DOD, USDA, DOI, Department of Veterans Affairs (VA)

Improve data interoperability to enhance information sharing

Implementer: Congress, HHS, DOD, USDA, DOI, VA, DNI

Establish a National Public Health Data System

Implementer: Congress, HHS, DOD, USDA, DHS, VA

Integrate data within the National Public Health Data System

Implementer: HHS

Continued

Secure data and ensure data integrity for the National Public Health Data System

Implementer: HHS, DHS

Authorize the Center for Forecasting and Outbreak Analytics

Implementer: Congress

Assess biosurveillance capabilities across the federal government

Implementer: Congress, HHS, DOD, USDA, DHS

Develop next-generation personal protective equipment

Implementer: Congress, HHS, DOD, NASA, DOL

Transfer technology for personal protective equipment throughout the federal government

Implementer: Congress, DOD

Support research on pathogen transmission in built environments

Implementer: Congress, HHS, DHS, ED, DOT

Develop and advance technologies that can reduce pathogen viability and transmission in built environments

Implementer: Congress, HHS, DHS, DOD, ED, DOT

Reduce pathogen transmission in built environments

Implementer: Congress, FEMA, General Services Administration (GSA), DHS

Review adequacy of biosafety and biosecurity standards, practices, and oversight to identify gaps, needs, and upgraded approaches

Implementer: HHS, National Science Advisory Board for Biosecurity (NSABB), DOD, DOE

Address laboratory biosafety and biosecurity challenges

Implementer: Congress, HHS, CDC, USDA

Develop and support implementation of a strategy to screen DNA synthesis providers and users

Implementer: Congress, OSTP, HHS, DOC

Require entities to purchase genetic material from verified vendors

Implementer: Congress, Purchasing entities

THE BIOLOGICAL THREAT LANDSCAPE

Biological threats to the Nation continue to expand and increase, multiplying so rapidly that current biodefense capabilities struggle to keep pace. About one million (more than 1 in 334) Americans have died.[15] Thousands still die every day as the virus continues to mutate and evolve. While optimism exists that we are on the threshold of the pandemic to endemic shift in COVID-19, we must be vigilant to monitor risk from additional SARS-CoV-2 variants. And yet, the pathogens that threaten us in the future may be deadlier and easier to transmit.

Other naturally occurring diseases persistently challenge countries and people throughout the world. We should not over-engineer or optimize our biodefense infrastructure by myopic focus on coronaviruses to the exclusion of all other pathogens. We need to recognize and address the diversity of potential biological threats. For example, we cannot ignore the relentless increase of antimicrobial resistance to existing therapies. Even if a virus causes the next pandemic, we will still need effective antibiotics to treat secondary bacterial infections, a leading cause of death during the 1918 influenza pandemic.

Humans, animals, and plants are all at biological risk. Interconnected transportation networks, food production methods, disruptive climate changes, poor land use practices, and increased or previously unusual human-wildlife interactions all contribute to the increasing risk and frequency of pandemics.[16,17] Zoonoses affecting humans and animals currently comprise 75 percent of emerging infectious diseases throughout the world.[18] As devastating as COVID-19 has been to our global and national economies, other microbial threats to human health could prove far worse. A disease affecting agriculture (e.g., African Swine Fever, wheat blast) could prove devastating.

The next biological event could be natural, human-generated, or accidental. As the scale and complexity of research studies on pathogens expands, the risk of potential laboratory accidents must be accorded appropriate assessment. In late 2019, a Brucellosis outbreak occurred at a vaccine production and research facility in Lanzhou, China, spread to more than 10,000 people, and extended into the following year.[19] In December 2021, the first local case of COVID-19 in over a month occurred after an infected mouse bit a worker in a high-containment laboratory in Taiwan.[20] As countries invest in building more laboratories, we can expect laboratory accidents to increase. At least 20 of the 59 Biosafety Level Four (BSL-4) laboratories worldwide were built in the past decade and most are located in densely populated areas.[21] Human error, limited understanding of how novel disease characteristics defy previously effective safety and security measures, and continued confusion about which biosafety level requirements apply to diseases that do not fit neatly into specific categories all challenge current laboratory biosafety and biosecurity programs. It is also easier now than ever[22] to obtain and modify pathogens, increasing the chances of pandemics due to laboratory accidents.

> Meanwhile, science is advancing far faster than our national determination to acknowledge the biological threat.

At the same time, the threat of a human-generated biological event continues to rise. While COVID-19 dominated worldwide attention, biological weapons programs rose to the fore once again. In April 2021, the Department of State (DOS) declared that Russia and North Korea possess and maintain active offensive biological weapons programs, that Iran has not abandoned its intent to conduct research and development of offensive biological agents, and that China has engaged in dual-use activities that may be in violation of the Biological Weapons Convention.[23] These programs obviously started well before the State Department made this statement. It is possible that Russia never ended its Soviet-era program, and for years, North Korea has essentially admitted its pursuit of the asymmetric advantage that biological weapons afford. According to Director of National Intelligence Avril D. Haines, the pandemic has driven China and Russia to gain geopolitical advantage through vaccine diplomacy and highlighted the importance of public health to national security.[24] Nation states and terrorist groups continue to develop and obtain advanced biotechnology in an effort to establish battlefield superiority, and the current conflict in

Ukraine raises global risks once again.[25] Dual-use science and technology research in the biological arena could help develop, produce, and maintain biological weapons.[26] Additionally, the lesser priority placed on counter- and nonproliferation of biological weapons allows these arms to race forward without the same impediments placed on other types of weapons of mass destruction.

Meanwhile, science is advancing far faster than our national determination to acknowledge the biological threat. Synthetic biology, genetic engineering, and the transdisciplinary convergence of biology with other fields (e.g., chemistry, engineering, computing, artificial intelligence (AI)) are advancing quickly. Concerns about security and health come up against the pursuit of science for the benefit of humanity. Policy and defense doctrine are not keeping pace. That lawmakers are only addressing the biosecurity implications of technologies such as the application of CRISPR-Cas9 (a technology widely used in the global research and development community), indicates that our lawmakers and agencies do not fully comprehend the scale of the biological threat or the rate at which it is growing.

Robust national biodefense must identify and defeat the diverse array of biological threats facing us. We can eliminate the threat of pandemics—whether natural, human-generated, or accidental—in ten years with The Apollo Program for Biodefense. The Athena Agenda provides recommendations and action items to ensure the Program moves forward.

ADVANCING THE APOLLO PROGRAM FOR BIODEFENSE

GOVERNANCE

The need to control COVID-19 created momentum to produce many technologies that we previously lacked the will and resources to pursue before the pandemic began. We need to build on that progress and push for technological advances to protect us from the next biological threat. These can come to fruition by the end of this decade, but only with leadership, resources, and interest that go beyond technical constraints and the usual crisis-neglect cycle timelines.

As with the effort to eradicate smallpox, we have the opportunity to do what once may have seemed impossible. We should not accept biological threats as inevitable when *The Apollo Program for Biodefense* can prevent outbreaks from spreading worldwide or occurring in the first place. While outbreaks may be inevitable, pandemics are not. The following ambitious recommendations have the potential to reshape our world if adopted and implemented fully.[27]

In September 2021, the Biden Administration released a plan to transform US capabilities to prevent, prepare for, and respond rapidly and effectively to, future pandemics and other high consequence biological events.[28] The American Pandemic Preparedness Plan addresses urgent needs and opportunities to protect the United States against biological threats and many of the technology priorities the Commission identified in its previous report, *The Apollo Program for Biodefense*. While the Administration requested $65.3 billion for this effort over 7 to 10 years, the Commission still believes that the appropriate amount is at least $10 billion a year, every year, for 10 years. The Commission recommended that a dedicated Deputy Assistant to the President within the National Security Council should lead the implementation of The Apollo Program for Biodefense, and that the Director of the Office of Science and Technology Policy should play an integral role in the prioritization and development of required technology capabilities for the Program.[29]

Building on the successes of Operation Warp Speed, we need to establish a sustainable system among the Department of Health and Human Services (HHS), Department of Defense (DOD), and other federal departments and agencies that enables the United States to respond rapidly to all biological threats and prevent deadly pandemics. This will require departments and agencies to evaluate their current biodefense capabilities and postures holistically within each organization,[30] and ensure centralized White House coordination of these activities.

The government must provide strong leadership, a clear mission, and sufficient resources to achieve The Apollo Program for Biodefense. An ambitious plan necessarily diverges from the *status quo*. The government must coordinate efforts, incentivize research, work with other countries, and ensure that each agency, company, nongovernmental organization, and laboratory understands how they fit into the plan to achieve this vision. Additionally, the government must ensure that technologies developed by The Apollo Program for Biodefense remain operational after the initial 10-year period has elapsed. Lastly, the public and private sectors must work together to find sustainable business models that support continuous defense against, and readiness to respond to, biological events. The Commission intends to address the critical need for private sector engagement in a separate report.

RECOMMENDATION: Fully Implement the *National Blueprint for Biodefense*.

The Administration and Congress should fully implement the Commission's 2015 *A National Blueprint for Biodefense* with special focus on the following recommendations and action items from that report:

- **Recommendation 27: Prioritize innovation over incrementalism in medical countermeasure development.**[31]
  - Prioritize innovation in medical countermeasures at agencies with biodefense responsibilities.
  - Exploit existing innovation.
  - Revolutionize development of medical countermeasures for emerging infectious diseases with pandemic potential.
  - Establish an antigen bank.
- **Recommendation 28: Fully prioritize, fund, and incentivize the medical countermeasure enterprise**.[32]
  - Fund the medical countermeasure enterprise to no less than authorized levels.
  - Reestablish multi-year biodefense funding for medical countermeasure procurement.
  - Address prioritization and funding for influenza preparedness.
  - Improve the plan for incentivizing the private sector and academia.

- **Recommendation 29: Reform Biomedical Advanced Research and Development Authority (BARDA) contracting**.[33] (*Note: Action Items a and c have already been accomplished*.)
  - Leverage previously provided authorities.
- **Recommendation 30: Incentivize development of rapid point-of-care diagnostics**.[34]
  - Develop requirements for rapid point-of-care diagnostics for all material biological threats and emerging infectious diseases.
- **Recommendation 31: Develop a 21st Century-worthy environmental detection system**.
  - Fund the development of advanced environmental detection[35] systems to replace BioWatch.
  - Replace BioWatch Generation 1 and Generation 2 detectors.
- **Recommendation 32: Review and overhaul the Select Agent Program**.[36]
  - Undertake a major reassessment of the Select Agent Program.
  - Overhaul the Select Agent Program.
- **Recommendation 33: Lead the way towards establishing a functional and agile global public health response apparatus**.[37]
  - Convene human and animal health leaders.
  - Establish the response apparatus.

RECOMMENDATION: Implement The Apollo Program for Biodefense (or its equivalent[38]).

White House initiatives enable the Executive Branch to embark on new programs without having to wait for months and years for dedicated congressional authorization. However, initiatives that are not congressionally authorized run the risk of ending if subsequent Administrations do not agree the program is needed. Developing a National Biodefense Science and Technology Strategy annex to the National Biodefense Strategy is a crucial first step towards creating the capabilities needed to defend against all biological threats and prevent pandemics in this decade.

- **Action Item a. Produce a National Biodefense Science and Technology Strategy.** The President should instruct the National Security Advisor, in coordination with the Director of the Office of Science and Technology Policy, to produce an annex to the National Biodefense Strategy that describes how the government will execute the 15 technology priorities found in The Apollo Program for Biodefense and assess its ability to leverage the private sector.[39] The National Security Advisor and Director of the Office of Science and Technology Policy should commence producing the annex immediately and complete it within 180 days.

- **Action Item b. Implement The Apollo Program for Biodefense (or its equivalent[40]).** Congress should amend the National Security Act of 1947 (P.L. 80-253, 61 Stat 495) to direct the National Security Advisor, in coordination with the Director of the Office of Science and Technology Policy, to authorize the Biodefense Steering Committee (previously established by the Trump Administration to oversee implementation of the National Biodefense Strategy) and establish an authorized subcommittee to oversee implementation of the National Biodefense Science and Technology Strategy annex to the National Biodefense Strategy. The Director of the Office of Science and Technology should chair this subcommittee, and members should include the Secretary of State, Secretary of Agriculture, Secretary of Defense, Secretary of Education, Secretary of Health and Human Services, Secretary of Commerce, Secretary of Homeland Security, Secretary of the Interior, Secretary of Labor, Secretary of Transportation, Administrator of the Environmental Protection Agency, Administrator of the National Aeronautics and Space Administration, Director of the Office of Management and Budget, Director of National Intelligence, and Director of the National Science Foundation. Congress should direct this subcommittee to implement the National Biodefense Science and Technology Strategy annex to the National Biodefense Strategy no later than two years following completion of the Annex.
- **Action Item c. Require a cross-cutting budget for The Apollo Program for Biodefense (or its equivalent[41]).** In accordance with Recommendation 4 of *A National Blueprint for Biodefense* to unify biodefense budgeting, Congress should amend the William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021 (P.L. 116-283) to require the Office of Management and Budget (OMB) to provide a cross-cutting budget for the National Biodefense Science and Technology annex to the National Biodefense Strategy as a component of the unified biodefense budget already required by law.[42] This budget submission should request additional dedicated funding—above existing biodefense funding—to support the implementation of the annex.

RECOMMENDATION: Provide appropriations to implement The Apollo Program for Biodefense (or its equivalent[43]).

Congress should provide funding to accomplish the goals of the Program and align it with the magnitude of current and future threats. Multi-year funding breaks the cycle of crisis/panic and neglect by providing predictable and stable time horizons for planning and investment in research, development, production, and work force recruitment and retention.

- **Action Item a. Appropriate funds for those federal departments and agencies that contribute to The Apollo Program for Biodefense (or its equivalent[44]).** Congress should appropriate funding to support implementation of the goals of the National Biodefense Science and Technology annex to the National Biodefense Strategy. Congress should align these appropriations with the annual unified biodefense budget submission and fund annex activities at no less than $10 billion each fiscal year. Critically, appropriations to support the Annex should add to—not supplant—existing federal biodefense funding, programs, and policies.

- **Action Item b. Provide multi-year budget authority.** Congress should include multi-year budget authority in appropriations for implementing the goals of the National Biodefense Science and Technology annex to the National Biodefense Strategy. The budget authority should cover annex activities for the next ten years. Congress should allocate this budget authority in accordance with the roles, responsibilities, and goals of the annex to facilitate long-term research, development, testing, and acquisition of biodefense technologies and medical countermeasures.

RECOMMENDATION: Produce a comprehensive mid- and post-crisis report on continuity of government for COVID-19.

Congress should amend the Robert T. Stafford Disaster Relief and Emergency Assistance Act (P.L. 100-707) to direct the Administrator of the Federal Emergency Management Agency, through National Security Council (NSC) coordination, to produce a comprehensive COVID-19 mid- and post-crisis report (including lessons observed) examining how COVID-19 affected each department and agency's operations and continuity of government as a whole. Agency internal evaluations provided to the Federal Emergency Management Agency (FEMA) should (1) address impacts on workforce management and safety, mission fulfillment, technology, and security; and (2) identify needed additional resources. Agencies should complete these evaluations within one year after enactment. Congress should direct the Administrator of the Federal Emergency Management Agency to use these agency internal evaluations and other information to produce a whole-of-government assessment and develop pandemic continuity of government recommendations. The Administrator should submit this assessment and recommendations to Congress and the Biodefense Steering Committee for incorporation into the National Biodefense Strategy within two years of enactment.

RECOMMENDATION: Revamp regulatory processes and policies to authorize or approve innovative technologies before, during, and after biological events.

The Food and Drug Administration (FDA) will play a significant role in reviewing many of the technologies that comprise The Apollo Program for Biodefense. FDA conducted a lessons-learned review through an independent organization as part of its Pandemic Recovery and Preparedness Plan Initiative.[45] FDA must move quickly to incorporate these lessons learned from the response to COVID-19 into its policies and practices, so that it can authorize or approve new diagnostics within days of the emergence of any new virus, variant, or mutation, and authorize or approve new vaccines and therapeutics within 100 days. To ensure public confidence in the safety and efficacy of the products the agency approves during public health emergencies, measures must be taken to create and institutionalize procedures and processes to insulate FDA experts and regulatory activities from undue political pressure.

- **Action Item a. Modernize and accelerate approval pathways for platform technologies to produce medical countermeasures.** Congress should amend the Public Health Service Act (P.L. 78-410) to direct the Secretary of Health and Human Services to further develop and implement a regulatory framework for review and approval of medical countermeasure platform technologies that (1) expedites approvals for platforms with validated safety profiles to rapidly deploy during a biological event caused by a novel pathogen; (2) incorporates lessons learned from the rapid authorization of COVID-19 mRNA vaccine platforms and the lack of rapid authorization of other platforms (e.g., monoclonal antibodies); and (3) sets clear requirements for the private sector to obtain authorization with this process. Congress should direct the Secretary to implement this process within one year of enactment.
- **Action Item b. Incorporate lessons learned from COVID-19.** Congress should amend the Public Health Service Act (P.L. 78-410) to direct the Secretary of Health and Human Services to implement lessons learned throughout the ongoing pandemic through regulations and subregulatory guidance to address how the agency can enhance its (1) ability to partner efficiently with the private sector in conducting real-time, rolling reviews of pre-clinical, clinical, and manufacturing data and by enhancing coordination across relevant agency centers for combination products and other products that require cross-center expertise; (2) communication and transparency with private sector sponsors and, as appropriate, the public, especially with respect to the types and specificity of data and goalposts needed for authorization of classes of medical products; (3) approaches to remote clinical trial mechanisms and inspections, including pre-established coordination mechanisms with foreign government inspection regimes; (4) facilitation of organized and prioritized clinical trial networks to rapidly test and evaluate potential vaccines and therapeutics; (5) capability, as appropriate, to evaluate vaccines, therapeutics, and other interventions for their potential to reduce transmission, in addition to their potential to reduce disease severity; (6) guidance on how to streamline development and regulatory review of modifications of previously authorized vaccines, therapeutics, and diagnostics to address changes in a dangerous pathogen over time, as well as second-generation products built using the same technological platform and/or combination vaccines addressing families of related viruses or variants—as either continuous development of the previously authorized vaccines or from a new vaccine standpoint; (7) guidance on how to develop vaccines and therapeutics for tropical or neglected diseases and combination vaccines for pathogens and/or variants that are on the US government's pathogen priority list; (8) use of predictive biomarkers, AI-based models, and real-world evidence to accelerate authorization of biomedical products, especially during a public health emergency, with established mechanisms to monitor and evaluate such use on a real-time basis; and (9) ability to insulate FDA experts from political pressure.

RECOMMENDATION: Develop a strategy and implementation plan for distributing at-home tests and therapeutics.

Congress should amend the Public Health Service Act (P.L. 78-410) to direct the Secretary of Health and Human Services, in coordination with the Postmaster General of the United States, to develop a strategy and implementation plan for rapidly deploying at-home tests and various forms (i.e. needle-free) of drugs and therapeutics directly to the public, using the United States Postal Service, within 48 hours of the declaration of a biological event by the Secretary of Health and Human Services. The Retail Pharmacy Program should assess the lessons learned so that a similar structure can be re-implemented when needed.

RECOMMENDATION: Support urgently needed public health research during biological events.

Congress should amend the Public Health Service Act (P.L. 78-410) to clarify that recipients of funding from the Public Health Emergency Fund can utilize it to fund time-sensitive research about an ongoing biological event that causes a public health emergency. Congress should authorize the use of this funding to investigate, collate, and analyze available information about the biological threat, transmission methods, mitigation measures, long-term mental and physical impacts on infected individuals, inequities in the application of public health measures, and other related issues. Congress should require the Secretary of Health and Human Services to submit a report to Congress regarding any such research funded by the Public Health Emergency Fund within 180 days of utilizing the Fund for this purpose.

RECOMMENDATION: Improve risk communications and build public trust.

Even with advances in technology, establishing public trust and communicating to the public challenged the United States throughout the pandemic. Guidelines consistently confused the public regarding masks, testing, vaccines, and other measures. The lack of public trust led to vaccine hesitancy and lower vaccination rates. Leveraging evidence-based methods for public communication to support policy is critical for public health. For example, an AI-powered interactive website answering common questions about Centers for Disease Control and Prevention (CDC) guidelines would help citizens know when to isolate and test after exposure based on user inputs.

- **Action Item a. Develop a strategy for crisis and risk communications that builds public trust**: The Secretary of Health and Human Services, in coordination with the White House and other departments, should develop a comprehensive strategy for risk communications and building public trust during biological events. This strategy should (1) contain an evaluation of lessons learned from risk and science communication failures throughout the COVID-19 pandemic; (2) provide evidence-based communication methods informed by current social and behavioral science research; (3) detail strategies to combat

misinformation; (4) identify technologies that could aid in delivering clear communications and guidance to the public; and (5) describe how to use social media and search engine platforms to improve communications. The Secretary should complete the strategy within six months and implement the strategy within one year of completion.

DEVELOP VACCINE CANDIDATES FOR PROTOTYPE PATHOGENS

Vaccine development is a time-consuming endeavor that has traditionally taken several decades per pathogen. Advances in many fields have enabled new approaches to vaccine development with much shorter timelines.[46] However, even with these innovations, vaccine development is a multi-step process that takes precious time.

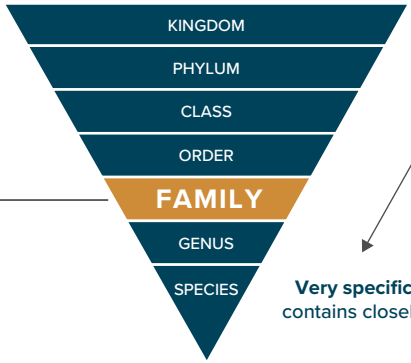
Fortunately, vaccine development for one pathogen is often translatable to other pathogens in the same viral family.[47] Thus, the extent to which we have previously invested in vaccine development against the same or related pathogens determines our capacity to rapidly develop a vaccine against a new pathogen.[48]

Although scientists frequently discover new viral species that infect humans, the number of viral families that these species belong to has plateaued. Therefore, by investing in vaccines for at least one prototype pathogen in each of the 26 viral families known to infect humans, we could reduce the global burden of infectious disease while simultaneously preparing for the next unknown biological threat. These efforts would also help develop a strong and diverse research community, better prepare us to address new threats rapidly as they emerge, and prevent the need for difficult and blunt interventions.

By investing in research and development at home and providing resources to international public-private partnerships, the United States could provide leadership and coordination globally, while also enabling the Nation's talent to lead scientifically. Operation Warp Speed demonstrated that new approaches in vaccine development (such as mRNA platform technology) can drastically shorten the timeline from decades to months. Operation Warp Speed has generated significant momentum for vaccine development capability that should continue beyond the COVID-19 pandemic to prevent the next.

We should continue research to validate generalizability. When we need to use the same vaccine approach in the future, rapid entry into Phase 1 clinical trials will be possible by leveraging data from previous clinical trials. For pathogens that are currently endemic and that frequently cause outbreaks, clinical trials should progress through Phase 2 and 3, to serve affected populations and provide a stronger basis for efficacy for a given vaccine design.[49]

Figure 3: Viral families of concern to human health.



26

Viral Families that Infect Humans


Adenoviridae


Anelloviridae


Arenaviridae


Astroviridae


Bornaviridae


Bunyaviridae


Caliciviridae


Coronaviridae


Filoviridaea


Flaviviridae


Hepadnaviridae


Hepeviridae


Orthomyxoviridae


Papillomaviridae


Paramyxoviridae


Parvoviridae


Picobirnaviridae


Picornaviridae


Pneumoviridae


Polyomaviridae


Poxviridae


Reoviridae


Retroviridae


Rhabdoviridae


Delta


Togaviridae

Viruses in the same family have similar features that can be targeted for medical countermeasure development.

Had we created a vaccine for SARS-CoV-1, a coronavirus that causes severe acute respiratory syndrome known as SARS, past early-stage development and animal studies, we could have produced a vaccine for SARS-CoV-2 even faster. Accordingly, having already developed a vaccine for SARS-CoV-2, we will be further ahead when we develop and trial vaccines for variants or other coronaviruses within that family. Moderna and the National Institutes of Health (NIH) developed the first batch of mRNA vaccine for SARS-CoV-2, just 25 days after China released the genomic sequence, and gave their first clinical trial participant a dose just 63 days later.

In March 2021, the Biden Administration proposed The American Jobs Plan which called for $30 billion in funding over four years (in addition to an initial investment of $10 billion from The American Rescue Plan) to protect against future pandemics.[50] Part of this funding would go towards the development of prototype vaccines through Phase I and II trials, test technologies for the rapid scaling of vaccine production, and sufficient production capacity in an emergency.[51] The Administration rolled this proposal into its September 2021 American Pandemic Preparedness Plan,[52] a 10-year $65.3 billion plan that also included dramatically improving and expanding our arsenal of vaccines, therapeutics, and diagnostics. In March 2022 at the Global Pandemics Preparedness Summit, the Coalition for Epidemic Preparedness Innovations similarly pledged $1.535 billion to develop effective vaccines within 100 days of identification of an epidemic or pandemic threat.[53]

RECOMMENDATION: Develop at least one vaccine candidate for each of the 26 viral families that infect humans.

Congress should amend the Public Health Service Act (P.L. 78-410) to direct the Secretary of Health and Human Services, in coordination with the Secretary of Defense and Secretary of Agriculture, to (1) identify at least one pathogen from each of the 26 viral families that affect humans to target for vaccine development, taking the diversity of viruses and priority pathogens into consideration;[54] (2) establish sustainable public-private partnerships with industry and academia for research and development; (3) develop a vaccine candidate for each viral family that infects humans; (4) advance vaccine development for endemic pathogens through Phase 2 and 3 clinical trials to serve affected populations; (5) advance vaccine development for pathogens that are not endemic through Phase 1 clinical trials to demonstrate safety; and (6) submit an annual progress report to Congress.

DEVELOP THERAPEUTIC DRUGS IN ADVANCE OF OUTBREAKS

At the very beginning of an outbreak of a novel pathogen, our best pharmaceutical line of defense will be those drugs that have either already been approved by the FDA, or those that have advanced far into clinical trials and can be rapidly deployed. For example, Remdesivir—a drug with a validated safety profile in Phase 1 clinical trials against

Ebola, and that had preclinical data showing activity against multiple viruses— including coronaviruses—was able to rapidly proceed into Phase 3 clinical trials and was the first drug to receive an Emergency Use Authorization from the FDA. While Remdesivir was not panacea for patients admitted to the hospital, previous trials made the rapid pace at which Phase 3 trials started possible. Unfortunately, drugs like Remdesivir are rare due to systematic underinvestment by the pharmaceutical industry in the development of treatments for acute viral diseases.

To ensure that we have a multitude of drugs ready at the beginning of the next pandemic, we need to make investments in the development of multi-pathogen therapeutics—those that can be effective against multiple phylogenies of viruses.[55,56,57] Previous efforts to develop multi-pathogen therapeutics have largely targeted direct-acting small molecule antivirals. However, new modalities are emerging that may result in increased breadth and potency and which warrant extra investment, including host-directed antivirals and monoclonal antibodies targeting regions conserved across multiple viral species.[58,59] Funding the development of a diverse repertoire of multi-pathogen therapeutics through Phase 1 clinical trials—and, for endemic pathogens that currently affect populations throughout the world, Phase 2 and 3 clinical trials—would ensure that we could treat patients as early as possible in an outbreak, no matter the pathogen. Also, we can gain valuable information about the process of drug development that would inform efforts to develop even more effective therapeutics after an outbreak has occurred and the specific viral pathogen identified.[60]

Since we are uncertain of what the next biological threat will be, the traditional approach of developing a therapeutic for a single virus after it emerges will not adequately prepare us. Multi-pathogen antiviral therapeutics could address a broad spectrum of viral pathogens, much like antibiotics can address multiple bacterial pathogens.

Some of this work is underway by federal agencies. Between 2011–2019, the National Institute for Allergy and Infectious Diseases (NIAID) invested about $245 million in research on broad-spectrum antiviral therapeutics.[61] This relatively small amount of funding helped to advance viral targeting.[62] In 2020 and 2021, the DOD Defense Advanced Research Projects Agency (DARPA) invested about $88 million in promising solutions through its Pandemic Prevention Platform program, which aims to develop a scalable adaptable, rapid response platform capable of developing sufficient medical countermeasures within 60 days of identifying a novel threat.[63,64] The Biomedical Advanced Research and Development Authority (BARDA) was well positioned to advance broad spectrum antiviral development, but before COVID-19 began, only 1.5 percent (1/67) of BARDA's grants or investments were for such therapeutics.[65] Additionally, congressional funding for BARDA is insufficient to accomplish their mission.

Existing examples of broad-spectrum antivirals include faviparavir and alisporivir.[66] The government of Japan approved faviparavir to treat multiple strains of influenza virus,

and clinical trials are ongoing to test its effectiveness against COVID-19.[67,68] Alisporivir is effective against dengue, SARS-CoV-1, and hepatitis C, yet industry decided to not pursue the drug because they questioned its profitability.[69,70] While an argument can be made for the federal government to pay entirely for the development of broad-spectrum antivirals, at the very least, the private sector needs advance market commitments and other incentives from the government to prevent market failures that could preclude such development.

RECOMMENDATION: Develop a suite of broad-spectrum antiviral drugs.

Congress should amend the Public Health Service Act (P.L. 78-410) to direct the Secretary of Health and Human Services, in coordination with the Secretary of Defense and Secretary of Agriculture, to (1) develop novel broad-spectrum antiviral therapeutics; (2) establish sustainable public-private partnerships with industry and academia for research and development; (3) advance antiviral development for endemic pathogens through Phase 2 and 3 clinical trials to serve affected populations; (4) advance antiviral development for pathogens that are not endemic through Phase 1 clinical trials to demonstrate safety; and (6) submit an annual progress report to Congress.

RECOMMENDATION: Develop a strategy for the rapid development of a virus-specific antiviral during an emerging outbreak.

The Secretary of Health and Human Services should develop a strategy for the accelerated development of a virus-specific antiviral against a novel and specific disease during an emerging outbreak. This plan should address: (1) research and development processes; (2) the pathway to provide resources to conduct emergency research; (3) public-private partnerships for accelerated development; and (4) regulatory considerations. The strategy should delineate roles, responsibilities, and timeframes for bringing antivirals to market under accelerated development. This strategy should be submitted to Congress no later than one year after enactment of this requirement.

DEVELOP FLEXIBLE AND SCALABLE MANUFACTURING OF PHARMACEUTICALS

Following the successful development of therapeutics and vaccines against a novel pathogen, they must be rapidly manufactured at scale, both initially for clinical trials and later for distribution to the public. Currently, many of the drug and vaccine modalities that we rely on are not readily amenable to both flexible and scalable manufacturing. Small molecule drugs often require multiple steps to synthesize, and each requires its own set of reaction conditions that may vary by temperature, pressure, and reagents, as well as different isolation and purification steps. As a result, manufacturing processes for small molecules are often specific to each drug, making it difficult to repurpose existing facilities to scale manufacturing of a new drug.

Recombinant proteins form the basis of the plurality of vaccine and therapeutic candidates developed specifically against COVID-19. While existing manufacturing infrastructure supports large-scale recombinant protein production, the need to use cell culture for their production increases the time required to produce each batch of vaccine. Also, each protein may require its own expression, isolation, purification, and formulation conditions, making it difficult to repurpose existing facilities for the development and manufacturing of a new recombinant protein. Recombinant protein-based vaccines were, therefore, months behind leading vaccine candidates in entering COVID-19 clinical trials.

These leading vaccine candidates largely rely on platform technologies (i.e., technologies that use the same processes for manufacturing, formulation, and delivery of a drug or vaccine against multiple different pathogens). Such platform technologies typically involve genetically encoding the therapeutic or vaccine candidate in mRNA, DNA, or a viral vector, enabling the production of different therapeutic or vaccine candidates simply by changing a genetic sequence.[71] As a result, a facility designed to manufacture a therapeutic or vaccine candidate using a platform technology against one pathogen could be quickly repurposed against a new pathogen without much need to make changes to physical infrastructure or established production processes.[72]

The US government should broadly invest in the advancement of platform technologies to ensure that therapeutic and vaccine candidates against the next pandemic pathogen can be rapidly manufactured at scale. Certain technical challenges that stand in the way of platform technologies becoming more broadly utilized could be overcome with further research. For example, unstable viral vectored and mRNA vaccines require constant refrigeration, complicating the logistics of their distribution to the public. Research into formulations that would reduce the dependence on a cold chain for distribution could significantly increase the utility of these vaccines. Also, mRNA and DNA vaccines had previously lacked significant validation in human clinical trials. Further clinical experience with these nucleic acid-based vaccines would allow us to iteratively improve their safety and efficacy profiles. Finally, while much research effort has gone towards the development of vaccine candidates that leverage platform technologies, the same cannot be said for therapeutic candidates that leverage the same technologies. Monoclonal antibodies are drugs that are currently produced as recombinant proteins, making them expensive and time-consuming to manufacture. If we develop and produce them using platform technologies instead, they might be significantly more scalable in a pandemic. We need further preclinical and clinical research to validate the applicability of platform technologies to the delivery of therapeutics.

With enough investment in their maturation, platform technologies might eventually become well-established as a means of producing pharmaceutical products during and between pandemics, ensuring that we would always have a large, manufacturing base that could be rapidly redirected to produce medical countermeasures at the beginning of a pandemic. Also, if we can build up a strong track record of safety and efficacy for a given

platform in the clinic, we can benefit from more flexible regulatory standards for products developed using that platform subsequently. Streamlining manufacturing and regulatory approval processes that platform technologies might enable could allow us to develop, manufacture, test, and distribute medical countermeasures in months, not years, ultimately saving countless lives and livelihoods in the next pandemic.[73]

One way in which HHS supports public-private partnerships is through Centers for Innovation in Advanced Development and Manufacturing (CIADMs).[74] DOD similarly supports Advanced Development and Manufacturing centers for medical countermeasures.[75] Unfortunately, CIADMs failed to deliver on the promise of rapid medical countermeasures manufacturing during the COVID-19 pandemic. Problems plagued the Centers, most notably quality control issues at one facility in 2021, Emergent BioSolutions, that resulted in a brief disruption to the manufacturing and supply of COVID-19 vaccines at a critical time in the response to the pandemic.[76] At the end of 2021, only one CIADM remains at the Texas A&M University System.[77] Over the past three decades, the government has repeatedly failed to establish these partnerships and facilities as envisioned.[78] In *Biodefense in Crisis,* the Commission recommended that the Secretary of Health and Human Services conduct a comprehensive review of existing medical countermeasure programs, including CIADMs.[79] The government must work to expand national capability to scale up manufacturing rapidly in response to future biological events, but also must learn from the problems with previously established CIADMs and apply those lessons learned to future initiatives.

The FDA supports flexible and scalable manufacturing of pharmaceuticals by issuing guidance on emerging technologies, reviewing and approving medical products, and advancing regulatory science.[80] However, the agency has limited experience with platform technologies for medical countermeasures. If existing or future platforms could quickly produce a vaccine or therapeutic in response to a novel biological threat, we must ensure that the FDA establishes clear regulatory procedures in place for review and authorization so that the public would benefit from their use.

RECOMMENDATION: Review previous advanced manufacturing capability efforts for technologies for medical countermeasures.

Congress should amend the Public Health Service Act (P.L. 78-410) to direct the Secretary of Defense and the Secretary of Health and Human Services to conduct a joint review of previous advanced manufacturing capability efforts. The review should (1) identify the problems and challenges that plagued previous efforts and their sustainability, especially within the context of the COVID-19 pandemic (including supply chain and stockpiling issues); (2) provide recommendations to address those problems; and (3) identify opportunities to modernize and improve manufacturing capabilities. The Secretary of Defense and Secretary of Health and Human Services should submit the review to Congress no later than one year after enactment.

RECOMMENDATION: Expand advanced manufacturing capability for platform technologies for medical countermeasures.

Drawing on the results of the joint review above, the Secretary of Defense and the Secretary of Health and Human Services should develop a plan to expand advanced manufacturing capability for platform technologies. The plan should (1) articulate how many advanced manufacturing centers the Nation needs to rapidly scale up production of medical countermeasures; (2) identify potential private sector partners who could host these centers; and (3) articulate how these centers should operate during non-crisis periods to ensure their ability to respond quickly during an emergency. Congress should also appropriate funding to support flexible and scalable manufacturing of medical countermeasures to meet future needs.

DEVELOP NEEDLE-FREE METHODS OF DRUG AND VACCINE ADMINISTRATION

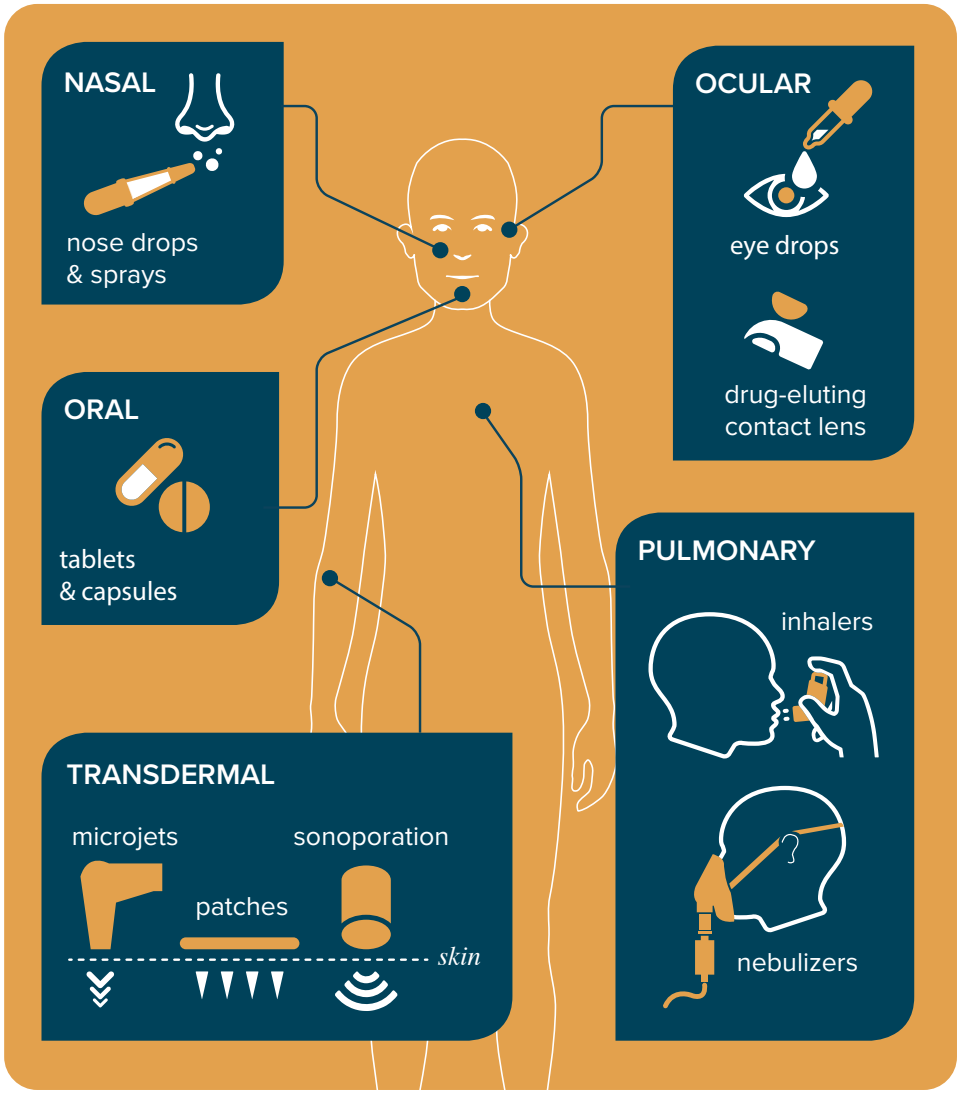
Once discovered, developed, and manufactured, we still need to distribute drugs and vaccines to the public. Today, most drugs and vaccines that would be useful during a pandemic require intravenous or intramuscular delivery—and thus, a healthcare provider to administer them. During a global pandemic, there may not be enough healthcare workers available to help treat or vaccinate the world's population, especially in countries with less-developed healthcare systems. Also, the widespread fear of needles reduces the population uptake of a new vaccine.[81] Thus, we need new methods of drug and vaccine delivery that would enable self-administration so that these medical countermeasures reach the most individuals possible.

Several different technologies exist that could facilitate the self-administration of drugs and vaccines. Microneedle patches—which are bandage-like patches that enable the simple delivery of a drug or vaccine through the skin—have been extensively investigated for influenza vaccine delivery, and have the advantage of reduced reliance on a cold chain for storage and transportation, and pain-free administration.[82] Intranasal or inhalable drugs or vaccines may also enable self-administration and would deliver the medical countermeasure to the respiratory tract, which would be of particular medical benefit against a respiratory pathogen.[83] Finally, while oral delivery is common for small molecule drugs, it has seen limited use with biologic drugs and vaccines. If technical barriers in oral delivery could be overcome, this method of administration could be the most readily adopted by patients. We could deliver self-administrable drugs and vaccines through the mail or patients could pick them up at their local pharmacy, greatly reducing the logistical challenges of delivering these pharmaceuticals to potentially billions of people.

The US government should invest in the advancement of the aforementioned technologies which enable transdermal (microarray patches), intranasal, inhalable, and oral delivery of drugs and vaccines. We can deliver pharmaceuticals that use these methods by developing

them for infectious diseases for which needle-based delivery is currently predominant (e.g., influenza, measles), which can serve as proving grounds for these technologies. We should advance these pharmaceuticals through at least Phase 1 clinical trials to enable timely evaluation of initial pharmacokinetics (for drugs) or immunogenicity (for vaccines). However, we should take care to ensure that any devices required for delivery are easy to use and manufactured on a large scale. With further advancement of self-administered vaccines, we could dramatically streamline the process by which we get life-saving treatments and vaccines to the public.[84]

Figure 4: Needle-free forms of drugs and vaccine administration.



Examples of promising technologies that could streamline the delivery of treatments and vaccines to the public include pain-free microneedle patches, delivery by mouth, delivery through the nose, and delivery through inhalation. These alternative methods allow for self-administration and have reduced logistical burdens associated with them, ensuring better public access. The federal government has funded limited work during the current pandemic toward these types of technologies. Aside from remdesivir, ritonavir-boosted nirmatrelvir (Paxlovid) and molnupiravir are the two authorized COVID-19 antivirals treatments available and both are oral pills. The US government purchased 20 million treatment courses of Paxlovid in late 2021.[85] BARDA,[86,87] the National Science Foundation (NSF),[88] and NIAID[89] have also invested in research on needle-free vaccines for diseases such as influenza and COVID-19. The BARDA Beyond the Needle program is developing technologies to make drugs and vaccines easier to administer and more widely available without needles and distribution burdens.[90]

RECOMMENDATION: Produce a research and development plan for needle-free methods of drug and vaccine administration.

The Secretary of Health and Human Services should, in coordination with the Secretary of Defense and Secretary of Agriculture, produce a plan for pursuing research and development of needle-free methods for drug and vaccine administration. The plan should address: (1) steps these departments will take to complete Phase 1 and subsequent clinical trials of newly developed technologies for currently circulating diseases like influenza and COVID-19; (2) lessons learned from those research efforts and their potential application to other pathogens; (3) how to coordinate these efforts with the prototype vaccine and antiviral initiatives recommended above; (4) research and development of new methods and capabilities for needle-free administration; (5) reformulation of current drugs and vaccines for needle-free administration; and (6) how needle-free delivery routes will be taken into consideration during the drug and vaccine development process.

IDENTIFY AND INCREASE UBIQUITOUS SEQUENCING

Nucleic acid sequencing (i.e., the reading of genetic material) is now widespread and has seen orders of magnitude decreases in cost, while simultaneously achieving increases in throughput. Sequencing provided the critical information to identify SARS-CoV-2 as a novel threat and enabled that information to travel around the world *faster* than the virus, enabling the design and manufacture of medical countermeasures. While impressive, it has substantially more to offer.

Metagenomic sequencing, the reading of all genetic material from a sample, offers advantages that many other capabilities struggle to rival.[91] All pathogens have

genetic material and produce tell-tale signs in an infected individual, known as host-responses. Sequencing allows us to read these signals, and is crucial for early detection, characterization of pathogens, epidemiological tracking, attribution, and development of other biotechnologies generally. Crucially, sequencing offers the ability to detect pathogens without looking for a specific threat, which is essential to identifying novel pathogens, whether natural or engineered.

Despite continued advances, often outpacing Moore's law, sequencing technology has critical bottlenecks to achieving the ubiquity, simplicity, and affordability needed.[92] If realized, sequencing could become routine in the clinical setting, as well as in high-risk low-resource areas of the world, expanding access to the most capable diagnostic tool. Sequencing could serve as the diagnostic for diseases generally and permit novel pathogen detection early and beyond our borders. All this, while also being robust against genetic changes in pathogens and offering the details needed to track, and ultimately reduce pathogen transmission.

To advance sequencing, we must increase investments in novel sequencing modalities, prioritizing methods enabling miniaturization and decreases in reagents or even reagent-free sequencing. Coupled with research and development focused on microfluidics and on-chip sample preparation, we can realize the vision of truly hand-held, affordable, easily operated sequencers. Decreasing the cost and applying advances in bioinformatics to the output would enable sequencing to become ubiquitous and permit the incorporation of sequencers into several products and settings that are currently prohibitive.[93] Sequencing broadly and frequently would provide a baseline understanding of the genetic material around us, permitting the early detection of new threats, while providing the critical diagnostic capacity needed to reduce the global infectious disease burden.[94]

The United States continues to lag behind other countries in terms of the number of virus genomes sequenced throughout the COVID-19 pandemic. For example, the United Kingdom sequences 9 percent of COVID-19 cases, while the United States only sequences 1 percent.[95] The United States also reports results more slowly and does not distribute sequencing capacity well (i.e., a small number of labs are doing much of the sequencing). While some technical bottlenecks remain in achieving an appropriately comprehensive sequencing capability, the United States can ramp up efforts significantly now and better engage existing capabilities. Essential efforts are underway to work with academic and public health laboratories, but fragmentation of the US healthcare system makes it difficult to collect information about samples. Furthermore, new strategies for undertaking genomic surveillance should be expanded. For example, the CDC has been trying to increase sequencing to track COVID-19.[96] The United States needs to expand its capability to monitor all pathogens, not just COVID-19. Towards that end, the American Rescue Plan contained $1.7 billion to strengthen and expand activities.[97]

RECOMMENDATION: Increase US sequencing capability and capacity.

Congress should amend the 21st Century Cures Act (P.L. 114-255) to direct the Secretary of Health and Human Services, Secretary of Defense, Secretary of Energy, and Secretary of Agriculture to develop a plan to increase pathogen agnostic metagenomic sequencing capability and capacity in the near- and long-term. The plan should (1) identify where sequencing capability and capacity currently lie in public sector laboratories, academic and research center laboratories, and other laboratory networks; (2) articulate how to identify sequencing capability and capacity in private sector laboratories; (3) provide an estimate of funding needed to expand capability and capacity in these laboratories; (4) explore the use of financial incentives to collect more samples in healthcare and wastewater settings; (5) set standards for the quality of information that should accompany each sample; (6) describe coordination with international partners to further sequencing development; and (7) describe how to achieve ubiquitous sequencing in the next five years. The Secretary of Health and Human Services, Secretary of Defense, and Secretary of Agriculture should deliver this plan to Congress within one year of enactment.

RECOMMENDATION: Identify the need for portable sequencing capabilities.

The Secretary of Health and Human Services should, in coordination with the Secretary of Defense, Secretary of Agriculture, and Secretary of Homeland Security, identify portable sequencing end-users and the sequencing capabilities they need in the federal government; states, localities, tribes, and territories (SLTT); healthcare settings; and ports-of-entry. The Secretary should take no longer than 180 days to identify these needs.

RECOMMENDATION: Develop affordable portable sequencing.

The Secretary of Health and Human Services should, in coordination with the Secretary of Defense and Secretary of Agriculture, develop a research and development plan that can make fielding portable sequencing in non-laboratory settings more affordable. The plan should (1) identify research efforts to produce portable sequencing devices in the public and private sectors; (2) address the miniaturization of these devices; (3) decrease or eliminate the reagents needed by these devices; and (4) address the integration of sequencing with microfluidics, on-chip sample preparation, and advances in bioinformatics. The Secretary should take no longer than one year to produce this plan.

DEVELOP MINIMALLY- AND NON-INVASIVE INFECTION DETECTION

The detection of an infection is most commonly pathogen-specific and initiated after the onset of symptoms or suspected exposure. Detection at this point is often too late and can miss both asymptomatic and pre-symptomatic infections where unsuspecting individuals may spread the disease further. In response to an outbreak, it should be

possible to deploy simple point-of-person tests to detect infections and guide resources for interventions, but these types of tests will not be available immediately. Even once they are available, tests will not be continuously conducted and must be done at some interval. New sensing capabilities, though, such as non-invasive volatolomics (the detection of volatile compounds emitted by an individual) and wearables could permit constant passive monitoring of markers of infection without interfering with or inconveniencing our daily lives. Furthermore, non-invasive and minimally-invasive detection techniques could provide avenues to monitor high-risk, high-concern, and sentinel populations for infections, without disrupting daily life.

We are on the verge of the ability to detect whether the body is currently infected with any pathogen, known or unknown, through the interrogation of host biomarkers. Increasingly, we can also detect infection indicators non-invasively through advances in wearables[98] and volatolomics.[99] These techniques can accurately measure digital biomarkers (e.g., physiological, biometric, biophysical, biochemical, mobility, and circadian rhythm changes) constantly and longitudinally, and detect subtle changes from an established baseline indicative of the onset of infection. This allows the device to prompt the user to change behavior or seek a clinical diagnosis.

Minimally invasive technologies (i.e., those that permit sample acquisition without pain, discomfort, inconvenience, or risk) would also facilitate molecular diagnostics for the identification of pathogens. This capability would allow for the detection of pre-symptomatic exposure, and asymptomatic infection and spread without the need for individuals to present in a clinical setting, allowing for early detection and substantially improved monitoring of novel biological threats.

Sensors are already shrinking in size, becoming more affordable, and increasingly capable. Yet, there is a need for more work on the integration and analytic systems that would permit drawing rapid inferences from them. We should make investments in the development of sensing and sampling capabilities, as well as testing of technologies to fully understand their potential and challenges. Additionally, particular attention should be given to the privacy of users of any device undertaking constant monitoring to prevent exploitation by malicious actors. If achieved, we could build the ability to detect novel and seasonal infections into our environment, while also facilitating advances in telemedicine and pushing capabilities into more austere areas.[100]

Throughout the COVID-19 pandemic, we have been primarily reliant on invasive methods of detection. For example, the National Aeronautics and Space Administration (NASA) received funding from HHS to develop a non-invasive detection method based on volatolomics to detect pathogens like COVID-19, called the E-Nose.[101] In the private sector, Ōura, the developer of a wearable smart ring, collects data from wearers to detect COVID-19.[102,103] Other examples of non- and minimally-invasive infection detection technologies include face masks that can detect the presence of pathogens, smart lenses

that can measure intraocular pressure, electronic tattoos that monitor stress markers, smart clothing that can measure skin temperature, smartwatches, and microneedle patches.[104] Despite promising preliminary data,[105] none of these technologies have yet matured to broader use by the public or health officials. These detection methods require further investment. The BARDA Division of Research, Innovation, and Ventures (DRIVe) program is working to advance such technologies through its Early Notification to Act, Control, and Treat program by partnering with innovators to develop non- and minimally-invasive technologies that enable early detection of biological threats.

For most of these technologies, privacy concerns and public participation must take into consideration during data collection. For example, small monetary incentives have been shown to increase public uptake.[106] The public sector must lay the policy groundwork to collect and aggregate data, build public confidence, engage with the private sector, and address privacy and incentive concerns.

RECOMMENDATION: Further develop the ability to detect infections with minimally- and non-invasive methods.

Congress should amend the Public Health Service Act (P.L. 78-410) to direct the Secretary of Health and Human Services, Secretary of Defense, and Secretary of Agriculture to (1) identify ongoing public and private sector research and development of minimally- and non-invasive infection detection technologies; (2) determine their potential for, and challenges with, utilization; (3) develop a funding plan to advance research and development in this arena; (4) identify the data sets and integration and analytics systems needed to draw rapid conclusions from these technologies; and (5) implement newly developed advanced technologies and methods of detection within three years from enactment.

DEVELOP MASSIVELY MULTIPLEXED DETECTION CAPABILITIES

Historically, diagnostic capabilities were specific to the pathogen, slow, and expensive. Single-pathogen diagnostics require clinical suspicion and are not readily available, or available at all, for some pathogens. If we suspect multiple pathogens, then we would need to run several assays, thereby increasing the cost and time to a diagnosis. Multiplexed detection capabilities address these challenges and bring new benefits by simultaneously testing for multiple pathogens, resistance genes, biomarkers, and analytes in a single simple assay.[107] Massively multiplexed detection capabilities in the form of pan-viral and pan-microbial assays have also been demonstrated, ushering in a new paradigm for diagnostics.[108]

Syndromic panels via multiplexed PCR assays (e.g., those used to test for approximately 25 of the pathogens most associated with respiratory infections) are currently available in many parts of the world, but do not include most known pathogens. While adequate for most

presentations of infectious disease, crucially, these panels do not cover less common and novel pathogens. Massively multiplexed panels can address these limitations by including virtually all known human pathogens and even detect novel pathogens based on conserved sequence homology[109] (i.e., the ability to detect similar regions in a pathogen's genetic tree). While the ability to detect almost any known pathogen is a tremendous advantage, for wide deployment, these arrays will need to become cheaper, more robust, simpler to operate, and faster. They must also achieve high sensitivity and specificity and ultimately be interpretable to clinicians.

To bring about these capabilities, the United States should make massively multiplexed assays a priority and provide funding for their research, development, and prototyping. New CRISPR-based massively multiplexed panels are particularly promising.[110] Other methods beyond these techniques have also been demonstrated previously, and new methods may also be possible. We should prioritize techniques enabling the tests to move out of centralized laboratories, and especially those that can operate in resource-constrained settings. The detection of viral pathogens for any host, including agricultural plants and animals, rapidly and with confidence would provide a capability to complement metagenomic sequencing and pathogen-specific point-of-person diagnostics.[111]

Research into these capabilities is currently ongoing through public-private partnerships established by DARPA, Defense Threat Reduction Agency, and NIH, and these technologies have advanced significantly throughout the pandemic.[112,113,114] DARPA should build on that progress by working to transition these technologies to others so they are sustained and further developed over time. NIH can also play a larger role in ensuring these capabilities realize their full potential through its Rapid Acceleration of Diagnostics (RADx) initiative.[115] BARDA seems well-positioned and can be more involved in advancing these detection technologies. As noted in the Commission's October 2021 report, *Saving Sisyphus: Advanced Biodetection for the 21st Century*, the Department of Homeland Security (DHS) is also involved and should further explore these capabilities to help defend the Nation against biological threats.[116]

RECOMMENDATION: Advance massively multiplexed detection capabilities.

Congress should amend the William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021 (P.L. 116-283) to direct the Secretary of Defense, in coordination with the Secretary of Health and Human Services and Secretary of Homeland Security, to develop and advance massively multiplexed detection capabilities. They should (1) assess ongoing research and development of massively multiplexed detection capabilities across the public and private sectors; (2) identify candidate technologies with the most beneficial performance characteristics for clinical applications, environmental monitoring, detection of novel pathogens by looking for conserved regions, identification of host-based biomarkers, and orthogonal detection mechanisms; (3) develop a five-year plan for funding research and development of such technologies in the public and private sectors; (4) submit an annual progress report to Congress detailing progress, current capabilities, and future directions for research and development; and (5) implement these technologies and methods within five years of enactment.

DEVELOP RAPID POINT-OF-USE DIAGNOSTICS

Rapid point-of-use diagnostics, also known as point-of-person or point-of-need diagnostics, are tests that can rapidly identify an infection wherever the individual is located. Point-of-use diagnostics stand in contrast to clinically administered diagnostics, which often require transportation to centralized laboratories, and days or weeks before rendering results.

In accordance with Recommendation 30 of the *National Blueprint for Biodefense*[117] and the recommendations made in *Diagnostics for Biodefense: Flying Blind with No Plan to Land*,[118] the Commission urges the US federal government to pursue rapid point-of-use diagnostics and the FDA to develop pathways for diagnostics to be approved for their public health potential to reduce community transmission.[119] Rapid testing can enable detection. Tests that take more than three days to produce a result are essentially useless in the context of outbreak control since beyond that point contract tracing becomes increasingly difficult.

Point-of-use diagnostics should be considered public health instruments, as opposed to simply clinical tools. Rapid tests should be readily available, minimally-invasive, portable, and user-friendly (i.e., easy to conduct and interpret). The end goal is to integrate point-of-person diagnostics with public health data systems. These tests can also extend testing to communities and populations that cannot readily access care.[120] Smartphone apps and other digital tools can aid in both the use and interpretation of results, as well as make results available to public health authorities. Rapid low-cost tests also allow for repeated use, which can be essential for novel pathogens with unknown incubation time, and for essential and frontline workers with multiple potential exposures. In the absence of such diagnostics, testing through a centralized laboratory will only increase the risk of spread by requiring individuals to present themselves publicly (especially in the case of extremely contagious pathogens). Additionally, a longer wait time places too much faith in a person's ability to quarantine for the appropriate duration.[121]

The United States experienced numerous challenges with the development, approval, manufacture, and distribution of new point-of-use diagnostic tests during the COVID-19 pandemic. Without these tests, we rely on centralized laboratory diagnostics that can sometimes take days to return results and initially took weeks, slowing response and the imposition of quarantine measures. Further, public guidance from federal agencies is muddled as to the use and interpretation of point-of-use tests, resulting in reduced test uptake, and preventing the types of public health screening initiatives deployed successfully in other peer countries.

RECOMMENDATION: Invest in point-of-use diagnostics.

The Secretary of Health and Human Services should (1) provide adequate funding to expand NIH RADx public-private partnerships in its annual budget request for the next five years; (2) invest in research and development of rapid point-of-use diagnostics for pathogens with

pandemic potential (in addition to COVID-19); (3) invest in research and development of diagnostics that test for multiple pathogens; (4) invest in research and development of nucleic acid based tests; (5) invest in research and development of rapid point-of-use diagnostic tests using a variety of sample types; and (6) invest in development of proven diagnostic technologies for widespread use against pathogens with pandemic potential.

RECOMMENDATION: Develop a plan for rapid development, approval, scaling, acquisition, procurement, and distribution of point-of-use diagnostic tests.

The Secretary of Health and Human Services should develop a plan to rapidly approve, develop, scale, acquire, procure, and deploy point-of-use diagnostic tests throughout the Nation in response to a biological event. The plan should (1) require the development of rapid point-of-use diagnostics following the initiation of diagnostics that require laboratory confirmation for a novel biological threat; (2) delineate the activities of the NIH RADx Executive Committee, Tech Governance Committee, Tech Working Group, and Underserved Populations Governance Committees[122] in engaging with DOD and the private sector to develop and scale diagnostic capabilities rapidly; (3) describe the processes for quick approval, acquisition, and procurement of rapid point-of-use diagnostics; (4) detail how these committees will rapidly deploy diagnostics across the country; (5) describe the process for making instructions easier to understand and less complicated; and (6) address simplified reporting to public health departments.

Develop a plan for rapid development, approval, scaling, acquisition, procurement, and distribution of point-of-use diagnostic tests.

ESTABLISH DIGITAL PATHOGEN SURVEILLANCE

Digital pathogen surveillance systems, which use internet-based and other electronically available data (e.g., medical bulletins, search queries, social media), have shown some improvement in recent years, including the provision of early warning signs for COVID-19. These systems, which have the potential for near real-time warning ability, international detection, and automated operation, could complement more traditional public health surveillance systems. With access to international airline routes, known disease networks, and anonymized mobility data, to name a few, we can predict the spread of infection and focus on resources and interventions in advance of outbreaks.

Limited access to information, poor integration of public and private data, and failure to bring the best talent and latest innovations to solve the problem of real-time digital surveillance

have limited the capability of extant systems to detect biological events early enough to respond effectively and contain the threat. By leveraging advances in machine learning, and in particular natural language processing,[123] we can continuously track vast amounts of data and filter the noise to provide relevant information to public health experts. This information is useful to prompt further investigation, allocate resources, and inform clinicians and public health authorities about potential pathogens to consider in their routine work.

The federal government should implement a system that monitors biological threats within and outside of US borders. We should leverage data sources (e.g., medical bulletins, livestock reports, satellite data, social media, online forums), in concert with the National Pathogen Surveillance and Forecasting Center ensuring data interoperability. The government should clear obstacles to access necessary data, incentivize innovation in the field through inducement prizes, and fund long-term efforts to continuously update the system with new data and capabilities as they become available.[124]

A few private sector companies have been using these technologies since the beginning of the pandemic.[125] In fact, BlueDot picked up a cluster of cases in Wuhan on December 30 and sent alerts to its customers nine days before the World Health Organization (WHO) alerted the world.[126] More government support and involvement are necessary to advance this technology and expand its availability. The HHS Office of the National Coordinator for Health Information Technology could assist with information sharing efforts,[127] and the Intelligence Community (IC) (e.g., the Office of the Director of National Intelligence Open Source Enterprise) could contribute to and reduce mis- and disinformation that corrupts this information flow with respect to biological threats.[128,129]

RECOMMENDATION: Invest in digital pathogen surveillance.

Congress should amend the Public Health Service Act (P.L. 78-410) to direct the Secretary of Health and Human Services, Secretary of Defense, Secretary of Agriculture, Secretary of the Interior, and Secretary of Veterans Affairs to (1) identify end-user needs for digital pathogen surveillance systems; (2) define clear performance requirements for the private sector; (3) provide incentives for the private sector to advance capabilities; (4) establish public-private partnerships with industry entities that have demonstrated pathogen surveillance capabilities; and (5) strengthen ongoing digital pathogen surveillance efforts throughout the government.

RECOMMENDATION: Improve data interoperability to enhance information sharing.

Congress should amend the Public Health Service Act (P.L. 78 -410) to direct the Secretary of Health and Human Services, Secretary of Defense, Secretary of Agriculture, Secretary of the Interior, and Secretary of Veterans Affairs, in coordination with the Director of National Intelligence, to develop a pathogen data interoperability plan to enhance information sharing among federal departments and agencies, the IC, industry, academia,

and nongovernmental organizations. This plan should (1) describe the structure of an information sharing network among these entities; (2) include data reporting standards to ensure interoperability; (3) consider the potential effects of cyberattacks and mis- and disinformation on these systems; and (4) implement this plan within one year of enactment.

DEVELOP A NATIONAL PUBLIC HEALTH DATA SYSTEM

As past outbreaks and the current pandemic have demonstrated, reliable, accurate, and comprehensive data is necessary for effective decision making during a crisis. Without timely and relevant information, it is not possible to prioritize resources and interventions, coordinate efforts, and respond in a manner the American people deserve. Although it is an enormous undertaking, a National Public Health Data System would provide the capabilities needed to effectively address the spectrum of biological threats.[130] To be successful, the system must be able to efficiently integrate, curate, and analyze data in a timely manner from federal, and SLTT public health agencies.[131]

The Coronavirus Aid, Relief, and Economic Security (CARES) Act provided the CDC with $500 million for public health data modernization and to support system-to-system interoperability and cloud-based centralized repositories. These efforts, while ongoing, will hopefully provide a strong foundation for future efforts to further ensure that data are simple to gather and deposit (while preserving privacy), available in real-time, and secured against cyberattacks. We should design continuous and timely integration of emerging technologies and data streams into the system from the start, with aims of reducing the burden of reporting and keeping outputs from the system simple to interpret and act on.

Our priority should be to establish and sustain a national and integrated public health data capability. With this foundation, we could integrate additional capabilities as they become available or advanced (e.g., digital pathogen surveillance, new streams of clinical and laboratory data, access to electronic health records, anonymized human movement, new visualization capabilities, improved analytics). The government should continue to prioritize public health data and sustain investments in both the maintenance and advancement of the system.[132]

Throughout the pandemic, the lack of a national public health data system to integrate and share information among SLTT and federal entities slowed response and left many communities blind to the spread of disease. It also prevented the establishment of an effective integrated national pathogen surveillance and forecasting capability.

The CDC launched the Data Modernization Initiative in 2020 to (1) strengthen data reporting, management, and analytics across federal and SLTT public health departments and agencies; (2) conduct improved and expanded surveillance of current and future public health threats; (3) help their staff pursue innovation and build state-of-the-art data science skills; (4) deliver guidance the public can trust by integrating nationwide standards for data access and

exchange; (5) bolster systems that link real-time data about emerging health threats; (6) create innovative pandemic-ready solutions for timely and complete data reporting to CDC; and (7) integrate nationwide standards for efficient and secure data access and exchange.[133] Unfortunately, CDC did not start the Initiative before COVID-19 began.

RECOMMENDATION: Establish a National Public Health Data System.

Congress should amend the Public Health Service Act (P.L. 78-410) to direct the Secretary of Health and Human Services, in coordination with the Secretary of Defense, Secretary of Agriculture, Secretary of Homeland Security, and Secretary of Veterans Affairs, to establish a national public health data system that expands on current data modernization efforts. They should (1) identify all relevant and available federal, SLTT, and private sector data streams; (2) determine and build the federal and SLTT technological capabilities needed to sustain the system over time; (3) ensure ease of data entry by including end-users in the development and beta-testing process; (4) de-identify personal data and protect privacy; (5) compile and integrate relevant data streams no later than two years after enactment; (6) ensure that the System will support timely and transparent access by the public; (7) provide funding and technical support to SLTT to enable them to contribute to this system; and (8) establish the system no later than three years after enactment.

RECOMMENDATION: Integrate data within the National Public Health Data System.

The Secretary of Health and Human Services should develop a plan to integrate data in the National Public Health Data System. The plan should (1) describe how information will flow and how federal, SLTT, academic, and healthcare entities will gather data; and (2) set data reporting and collection standards to ensure interoperability.

RECOMMENDATION: Secure data and ensure data integrity for the National Public Health Data System.

The Secretary of Health and Human Services should, in coordination with the Secretary of Homeland Security, develop a data security and integrity plan for the National Public Health Data System. The plan should (1) describe how HHS and DHS will secure and defend the System against cyberattacks; and (2) address how HHS and DHS will prevent and respond to the introduction of mis- or disinformation into the System.

ESTABLISH A NATIONAL PATHOGEN SURVEILLANCE AND FORECASTING CENTER

An integrated real-time national pathogen surveillance and forecasting center with advanced capabilities to detect and model naturally occurring, accidentally released, and intentionally introduced biological threats does not currently exist. The abilities to identify and forecast threats rapidly is critical at the beginning of an outbreak and the understanding of infectious

disease prevalence, including seasonal pathogens, are essential components of public health planning and response.[134] Aggregating diverse data sources in real-time and forecasting infectious disease outbreaks are necessary to prevent or rein in the spread of biological threats. Improved forecasting through modeling also allows for better projection of the pandemic potential that a threat poses and aids in the prioritization of resources, mobilization of a response, and initiation of countermeasure development and deployment.[135]

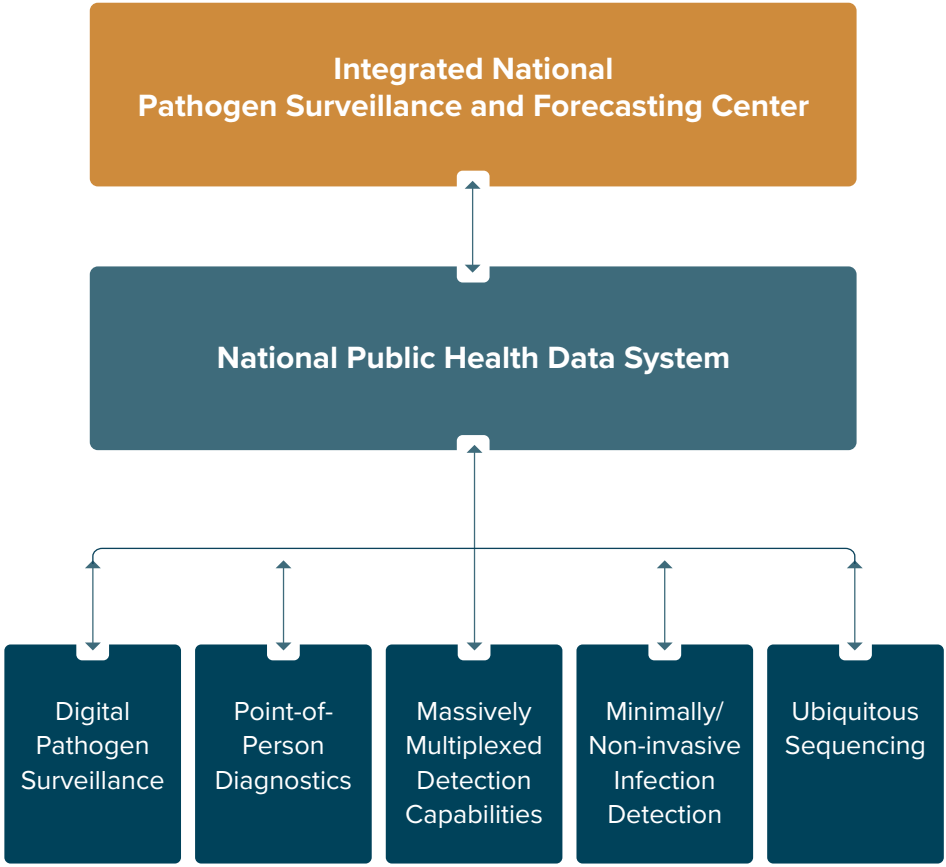
Current infectious disease forecasting capabilities rely on data that are sometimes unavailable for weeks. An assortment of academic groups usually coordinates to create a forecast, but they must be able to gather and analyze data quickly for it to be accurate and useful. The United States should be ahead of the curve, take these threats more seriously, and establish a permanent National Pathogen Surveillance Forecasting Center. This center would maintain forecasting capacity, improve science, and invest resources in the building and maintenance of the best models, pipeline, and community of researchers. Furthermore, the Center should integrate the National Public Health Data System and aggregate information from clinical molecular diagnostics, distributed sentinel surveillance, digital pathogen surveillance, laboratory biosafety monitoring, and animal and environmental pathogen surveillance. This would allow for improved detection of novel biological threats and a better understanding of rapidly evolving outbreaks and attacks.

Effective modeling also requires reliable data and a thorough understanding of pathogen transmission and available public health interventions. Additionally, it is also necessary to have data on historical trends of transmission, population mobility, and individual decisions in response to public health threats.[136] Forecasting success will also depend on the ability to communicate and relay relevant information in an effective manner (e.g., through visualizations or other dashboards) to decision makers. As some have noted, weather forecasting through the National Weather Service successfully takes advantage of, and integrates data from automated weather stations, radar sites, and satellites; maintains archival data; and progressively improves forecasts.

The ability to forecast the trajectory of a pathogen rapidly and reliably is crucial for the United States to address seasonal infectious diseases, and to prepare for and respond to emerging and engineered threats. By establishing a National Pathogen Surveillance and Forecasting Center as a permanent federal institution, the United States could advance these capabilities and ensure future preparedness.[137]

The CDC established the Center for Forecasting and Outbreak Analytics in August of 2021 to inform public health decision making. The American Rescue Plan provided the Center with initial funding to predict outbreaks through modeling and forecasting, expand data sharing and integration, establish standards to maximize data interoperability, and communicate results to stakeholders.[138] DOD, the national laboratories, and the private sector could all assist in the development of accurate forecasting algorithms for the Center to use. The Center would also benefit from the integration of, and access to, data generated throughout the government.

Figure 5. Data collected from relevant Technology Priorities should feed into a National Public Health Data System and used for pathogen surveillance and forecasting.



RECOMMENDATION: Authorize the Center for Forecasting and Outbreak Analytics.

Congress should amend the Public Health Service Act (P.L. 78-410) to authorize the Center for Forecasting and Outbreak Analytics.

RECOMMENDATION: Assess biosurveillance capabilities across the federal government.

Congress should amend the Public Health Service Act (P.L. 78-410) to direct the Secretary of Health and Human Services, in coordination with the Secretary of Defense, Secretary of Agriculture, and Secretary of Homeland Security, and in collaboration with the national laboratories and the private sector, to (1) assess biosurveillance capabilities and relevant data

streams across the government to incorporate into the Center for Forecasting and Outbreak Analytics; (2) develop effective algorithms that produce accurate forecasts for the Center; (3) request an annual review by the National Laboratories and National Academies of Sciences to help identify problems, challenges, and potential improvements, and provide technical assistance to the federal government; (4) develop an interoperability strategy for integrating data into the Center; and (5) develop plans to ensure data interoperability and integration, provide data security and integrity, prevent and respond to cyberattacks on the Center, and prevent and respond to the introduction of mis- or disinformation into the Center's data streams.

DEVELOP NEXT-GENERATION PERSONAL PROTECTIVE EQUIPMENT

Personal protective equipment (PPE) can be used to protect against a broad-spectrum of biological threats. However, the current state of PPE burdens its users, requires experience in proper usage, is seldomly reusable, is not widely available to all populations, and does not properly fit everyone (e.g., children).[139] Additionally, since the primary goal of PPE is to prevent the wearer from becoming infected, not enough emphasis has been placed on preventing the wearer from infecting others. Shortages of PPE leave frontline and essential workers at risk, threatening their health and reducing their capacity to respond.

The COVID-19 pandemic has highlighted limitations in our knowledge of PPE and exposed an inadequate ability to rapidly scale up production. However, the pandemic has also catalyzed efforts to make PPE reusable, spurred new ideas about respirator designs, seen the advent of personalized PPE, and eventually brought new production capacity to fruition. While these efforts mark advancements, focused research efforts and innovative approaches could achieve much more.

To develop the next generation of PPE, we should make innovations in the following areas: 1) reusable, sterilizable, and self-disinfecting equipment; 2) modular designs responsive to a wide range of threats, including those which go beyond biological threats; 3) personalization to ensure adequate protection, comfort, and attractiveness; 4) rapid production from widely available materials without supply vulnerabilities; 5) the ability to neutralize pathogens; 6) sensing capabilities to detect potential exposures; and 7) protection beyond traditional masks, respirators, gloves, gowns, etc., that safeguard the wearer without burden. The government should invest in and incentivize the development of these PPE innovations through inducement prize challenges, intramural and extramural research and development efforts, advance purchase commitments and consistent acquisition, and use-inspired basic research programs, such as DARPA's Personalized Protective Biosystem effort. Establishing distributed capacity will ensure PPE is available in advance, and maintaining capability will ensure increased production and surge in response to a threat. Additionally, the government should develop standards and metrics for the evaluation of all forms of PPE to quantify capabilities, standardize comparisons, and assess progress.[140]

The government has invested in the research and development of next-generation PPE. For example, NIH invested in the research and development of a smart mask that changes colors when exposed to COVID-19.[141] A team at the NASA Jet Propulsion Laboratory developed a 3D printable Powered Air-Purifying Respirator with custom filters and commercial off-the-shelf components to help provide more PPE during the COVID-19 pandemic,[142] making the design, components, and production guide openly available. NASA also worked with hospitals during the pandemic to develop new methods and technologies for decontaminating PPE.[143] Additionally, the private sector also invests in developing next generation PPE.[144] In fact, many companies participated in the 1448 submissions to the "Mask Innovation Challenge: Building Tomorrow's Mask", led by BARDA DRIVe and the National Institute for Occupational Safety and Health, to develop innovative masks to provide protection from respiratory pathogens such as SARS-CoV-2.[145] However, the government needs to update standards for public use of PPE (e.g., cloth masks) to ensure adequate protection against infectious disease threats.

RECOMMENDATION: Develop next-generation personal protective equipment.

Congress should amend the Public Health Service Act (P.L. 78-410) to direct the Secretary of Health and Human Services, in coordination with the Secretary of Defense, the Secretary of Labor, and the Administrator of the National Aeronautics and Space Administration, to (1) assess ongoing research and development of next-generation PPE in the public and private sector; (2) provide a funding plan for advancing research and development in the public and private sectors; (3) clearly provide criteria and metrics to the private sector; and (4) develop next generation PPE for use in healthcare settings and against biological threats within one year of enactment.

RECOMMENDATION: Transfer technology for personal protective equipment throughout the federal government.

Congress should amend the Stevenson-Wydler Technology Innovation Act of 1980 (P.L. 96–480) (94 Stat. 2311) and the Federal Technology Transfer Act (P.L. 99-502), 15 U.S.C 3710 to direct the Secretary of Defense to establish a technology transfer center to facilitate the sharing of PPE technology with and by other federal departments and agencies, and the private sector.

SUPPRESS PATHOGEN TRANSMISSION IN THE BUILT ENVIRONMENT

Transmission of most known pathogens occurs in human-built environments (e.g., offices, healthcare facilities, schools, public transportation, planes) via air, droplets, and fomites.[146] While we have exerted significant effort to engineer and make the built

environment robust against fires, earthquakes, and other threats, we have put little effort into engineering and making our world robust against pathogens. Suppressing pathogen transmission, especially in high-risk and high-traffic spaces, would reduce the spread of infectious diseases, extinguish some outbreaks, and buy critical time to combat more aggressive pathogens. With permanent incorporation into the environment, we could continuously defend against threats, even prior to detection, and without the dramatic changes in human behavior needed to reduce pathogen transmission.[147]

To reduce the effective transmissibility of most airborne, droplet, vector-borne, and fomite transmitted pathogens, we should make investments in:

- affordable air filtration and sterilization systems
- deliberate design of airflows
- self-sterilizing surfaces
- easily sterilized materials, robust against harsh sterilization
- robotic and autonomous integrated sterilization
- fomite neutralizing technologies
- integrated real-time pathogen sensing capabilities

Conducting pilot studies in select high-risk environments would help to achieve a deeper understanding of how to re-engineer the built environment to reduce pathogen transmission before eventually expanding implementation throughout all population dense environments in the Nation. We should fund research and development efforts to foster a field of study and discover innovative technologies to further advance capabilities. As part of a modernization effort, the federal government should invest in technologies to retrofit current infrastructure, such as HVAC systems and public transport, and incentivize the incorporation of suppression technologies into new production through tax credits and grants, before ultimately incorporating proven aspects into regulation.[148]

During the course of the COVID-19 pandemic, the government has helped strengthen the built environment against pathogen transmission by retrofitting existing, and setting standards for new, infrastructure. For example, several recent stimulus packages provided significant funding to schools to help retrofit their buildings for safe in-person learning during COVID-19,[149] although it is unclear the extent to which these investments were targeted and whether congressional and federal oversight was sufficient.[150] The General Services Administration (GSA)[151] and the DHS Cybersecurity and Infrastructure Security Agency could play a larger role in reducing pathogen transmission in the federal built environment. Further, since the private sector possesses many applicable technologies,[152] the government should establish partnerships with industry and academia for research, development, acquisition, and procurement of technologies.

RECOMMENDATION: Support research on pathogen transmission reduction in built environments.

Congress should amend the Public Health Service Act (P.L. 78-410) to direct the Secretary of Health and Human Services, in coordination with the Secretary of Homeland Security, Secretary of Education, and Secretary of Transportation to produce a research and development plan for reducing pathogen transmission in built environments, including transportation environments such as vehicles, buses, trains, and planes. The plan should (1) provide an assessment across the federal government and private sector of ongoing technology research and development for reducing pathogen transmission in built environments, including monitoring and detection technologies; (2) include a funding plan for advancing research and development in the federal government and incentivizing the private sector to engage in research and development (including pilot programs); (3) articulate criteria and metrics to measure, monitor, and assess the success of how well certain technologies reduce pathogen transmission in built environments; and (4) include a timeline for implementation within one year of enactment.

RECOMMENDATION: Develop and advance technologies that can reduce pathogen viability and transmission in built environments.

The Secretary of Health and Human Services, in coordination with the Secretary of Homeland Security, the Secretary of Defense, the Secretary of Education, and the Secretary of Transportation should (1) establish a program to develop and refine technologies that reduce pathogen transmission in built environments, including transportation environments such as vehicles, buses, trains, and planes; and (2) develop building code standards that apply these technologies and pathogen reduction best practices. Congress should amend the Public Health Service Act (P.L. 78-410) to require the Secretary to submit a progress and findings report within one year of enactment and annually thereafter.

RECOMMENDATION: Reduce pathogen transmission in built environments.

Congress should amend Homeland Security Act (P.L. 107-296) to (1) require SLTT to update building codes to factor in standards and requirements for reducing pathogen transmission in newly built environments, including transportation environments such as vehicles, buses, trains, and planes, as a requirement for participation in the Homeland Security Grant Programs administered by FEMA; (2) authorize appropriations to retrofit existing GSA and other federally owned and leased facilities to reduce pathogen transmission in the built environment; and (3) establish a federal grant program administered by FEMA to offer assistance to SLTT to reduce pathogen transmission in their built environments.

ESTABLISH COMPREHENSIVE LABORATORY BIOSAFETY AND BIOSECURITY

While high-containment laboratories already have an impressive number of safeguards in place, they could benefit from continuously updated research given the high risks involved. Recent biosafety lapses have included smallpox, anthrax, and contagious strains of influenza.[153,154] Indeed, some believe the 1977 H1N1 pandemic arose from a lab accident or botched vaccination experiment.[155] Additionally, the recent rapid proliferation of pandemic research has implications for dual-use risks and laboratory biosafety.[156]

Our risk tolerance in laboratories worldwide[157] working with biological threats should be comparable to that of air travel, where safety is engineered into the airlines and airports, and monitoring occurs constantly to detect and prevent human-generated and technology-based accidents. A constant focus on and prioritization of safety ensures that the complex and previously risky nature of flight can be undertaken safely.

We continuously innovate automobile safety technologies (e.g., lane departure warnings, blind spot monitoring, pedestrian detection). We should apply a similar approach to laboratory biosafety. This includes the refinement of current capabilities, analogous to advances in airbags for automobiles, to the introduction and rigorous testing of new technologies. Ultimately, we may realize the benefits of high-containment laboratory work while minimizing the risks to the greatest extent possible by developing pathogen monitoring capabilities, improved engineering controls, and risk assessment and analysis tools.[158] While training personnel is essential and the core of biosafety,[159] insider threats should also be more seriously considered, and safeguards put in place to deter and prevent any malicious behavior.

Additional funding is necessary for the study of laboratory accidents and the development and testing of new capabilities and tools to achieve comprehensive laboratory biosafety systems.[160,161] These should be tested in safe environments, continuously incorporated into current high-containment labs, and ultimately integrated into all biosafety labs.[162]

The Department of Labor (i.e., Occupational Safety and Health Administration); HHS (CDC and NIH); United States Department of Agriculture (USDA) Animal and Plant Health Inspection Service; Department of Transportation (DOT); and Department of Commerce (DOC) are primarily responsible for the regulation and oversight of the possession, use, or transfer of infectious agents, toxins, or other biological hazards.[163] Additionally, the NIH National Science Advisory Board for Biosecurity (NSABB) addresses issues related to biosecurity and dual-use research at the request of the United States Government.[164]

The Nation's BSL-4 laboratory operators need to come together in coordination with the CDC to determine how to ensure best safety practices, including greater transparency regarding accidents in these facilities, incentivize accident reporting and data collection, and strengthen laboratory biosafety and biosecurity through policy adjustments and innovative technologies. The increasing risk of a catastrophic accidental release from one of these laboratories means regulators must implement changes now before a disaster occurs. HHS,[165,166] DHS, DOD, and USDA should invest more in research to improve laboratory biosafety and invest more to ensure appropriate facility maintenance, workforce training, and practice oversight.

RECOMMENDATION: Review adequacy of biosafety and biosecurity standards, practices, and oversight to identify gaps, needs, and upgraded approaches.

The Secretary of Health and Human Services, in partnership with the DOD and Department of Energy (DOE), should request the NSABB to assess (1) the potential for innovation in laboratory biosafety; (2) potential outcomes of those innovations; and (3) current goals for next-generation technology in laboratory biosafety. The Secretary should take no longer than 180 days to complete this assessment.

RECOMMENDATION: Address laboratory biosafety and biosecurity challenges.

Congress should amend the Public Health Service Act (P.L. 78-410) to direct the Secretary of Health and Human Services, in coordination with the Secretary of Agriculture, to conduct an annual review of laboratory biosafety capabilities and challenges. The Secretaries should direct the Director of the Centers for Disease Control and Prevention to (1) conduct this review in coordination with at least one representative from each BSL-4 laboratory in the country; (2) identify potential innovations and policies to improve laboratory biosafety; (3) articulate ongoing challenges in laboratory biosafety, especially with regard to accident prevention, accident reporting, and needed funding for accident detection; and (4) provide goals and milestones for implementing improvements. The Secretary of Health and Human Services should complete the first review within 180 days of enactment.

TECHNOLOGIES TO DETER AND PREVENT BIOLOGICAL ATTACKS

The ability to investigate, analyze evidence, and attribute deliberate biological events is essential for both deterrence and response to a deliberate or accidental threat.[167] As tools are developed and the barriers to engineering pathogens continue to decrease, the number of possible actors may increase. Technologies are required to ensure safety is built in and capabilities developed in advance to prevent and deter action.

Unfortunately, biological attribution, genetic engineering detection, and microbial forensic techniques have only made small strides since the anthrax attacks of 2001. In the two decades since, there have been advancements in machine learning and physical characterization techniques, and artificial intelligence evolved from an "AI winter" to "AI summer." However, we have yet to see these technologies extensively applied, despite recent academic studies and government programs hinting at their impressive capabilities.[168,169] In particular, it should be possible to harness advances in machine learning techniques from several disciplines and apply them to distinguish natural and engineered DNA and to inform attribution. Training these machine learning tools will require access to relevant datasets which we must establish in advance.

Once developed, these capabilities could be broadly deployed and integrated into routine laboratory, clinical, and environmental settings as sentinels monitoring for engineered pathogens, in addition to being available for forensics applications. To advance these techniques, the federal government should make use of its investment capability and inducement prizes, as this would encourage the application of their capabilities developed for other applications to these problems. With additional dedicated funding to research, develop, acquire, and operate such technologies, as well as maintain the relevant repositories, we could establish a robust and known capability to detect, analyze, and attribute biological threats.[170]

The public and private sectors can leverage ongoing research and development to further biological attribution technologies. The Intelligence Advanced Research Projects Activity has seen success developing these technologies through its Functional Genomic and Computational Assessment of Threats (known as Fun GCAT) and Finding Engineering-Linked Indicators (known as FELIX) programs.[171,172] The private sector has successfully used prize competitions to significantly advance biological attribution technologies,[173] and some organizations have provided detailed roadmaps for broad-scale implementation.[174]

While these technologies show great promise, there is no up-to-date guidance or set of requirements for their use. For example, HHS issued guidance (with no requirements) for DNA synthesis providers in 2010.[175] But without a legal requirement saying otherwise, a bad actor can simply order malicious DNA from a company that does not screen their

customers or orders. Some State governments (e.g., in California[176] and Maryland[177]) recently considered establishing requirements for providers. They would require providers to register with either the International Gene Synthesis Consortium (IGSC)[178] or a health department to confirm they meet or exceed IGSC standards. The government should use these state efforts to inform development and implementation of national standards. Ideally, federal agencies would at least require any entity receiving a grant in the life sciences to purchase their synthetic DNA from an IGSC or federally approved vendor.

RECOMMENDATION: Develop and support implementation of a strategy to screen DNA synthesis providers and users.

Congress should amend the National Science and Technology Policy, Organization, and Priorities Act of 1976 (P.L. 94-282) to direct the Director of the Office of Science and Technology Policy to develop an updated screening framework with requirements for providers and users of synthetic biology services that meet or exceed those of the current gene sequence and customer screening best practices. Congress should amend the Public Health Service Act (P.L. 78-410) to direct the Secretary of Health and Human Services, in coordination with the Secretary of Commerce, to implement the framework.

RECOMMENDATION: Require entities to purchase genetic material from verified vendors.

Congress should amend the William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021 (P.L. 116-283), the Public Health Service Act (P.L. 78-410), the Homeland Security Act (Public Law 107-296), the Agriculture Improvement Act of 2018 (P.L. 115-334), and the National Science Foundation Act of 1950 (P.L. 81-507) to require any entity receiving a federal grant or engaging in a cooperative agreement related to synthetic DNA and RNA to purchase their synthetic materials from vendors that follow gene sequence and customer screening best practices to minimize risk and that address gene synthesis screening, customer screening, record keeping, order refusal and reporting, and regulatory compliance.[179]

CONCLUSION

In this Athena Agenda, we have offered recommendations with identified executors to advance The Apollo Program for Biodefense (or its equivalent) and achieve its mission to take pandemic threats off the table within the next 10 years. Now is the time to embark on this mission.

We can choose how we will manage biological risk. Within weeks of recognizing the existence of SARS-CoV-2, scientists mapped its entire genome and proceeded to develop and produce vaccines faster than ever before. They accomplished these previously unimaginable feats because of forward-looking programs, such as the Human Genome Project.

We have the opportunity today to implement in The Apollo Program for Biodefense (or its equivalent) and accomplish a grand mission that will:

- Save millions of lives
- Reduce the risk of hospitalization and disabilities
- Greatly improve and accelerate pharmaceutical manufacturing of breakthrough drugs
- Develop needle-free methods of delivery that decrease vaccine hesitancy
- Identify infectious disease outbreaks and the pathogens that cause them within hours of occurrence
- Test for hundreds of different pathogens with a single diagnostic
- Obtain rapid test results in less than 15 minutes
- Increase non-federal biosurveillance data
- Forecast infectious disease cases and deaths into the future
- Develop air filtration with the ability to reduce biological aerosols almost entirely

In this Athena Agenda, we have offered recommendations with identified executors to advance The Apollo Program for Biodefense (or its equivalent) and achieve its mission to take pandemic threats off the table within the next 10 years. Now is the time to embark on this mission—not only because it will achieve the goal of a pandemic-free world, but also because we can implement many of the components of The Apollo Program for Biodefense immediately to address our shortcomings in combatting the COVID-19 pandemic. Leaders around the world must take a hard look at the past two years and decide if the death and suffering so many people have endured is an experience worth risking again—especially as the biological threat continues to grow. The pandemic revealed our innovative powerhouse. The Apollo Program for Biodefense is unquestionably feasible if America commits to take on this grand challenge for the protection of life and the betterment of humanity.

We are at a turning point and closer to ending pandemics today than many would think. It is time to harness America's ingenuity, optimism, and wealth to achieve victory over biological threats.

APPENDIX A: GAPS AND SHORTCOMINGS IN BIODEFENSE

We are at the mercy of biological threats and associated health, economic, and other devastating consequences if we do not address the glaring gaps and shortcomings that prevent us from defending the nation against biological threats. Biodefense suffers constantly from a lack of adequate time, investment, innovation, capability and capacity, preparedness, quick response ability, data, and governance. If we are to execute The Apollo Program for Biodefense and achieve its mission to eliminate pandemics in 10 years, we must fill these gaps and eliminate these shortcomings.

LACK OF TIME

The development of new vaccines, therapeutics, other medical countermeasures, laboratory diagnostics, and biosurveillance systems takes far too long to enable quick response. For example, even with Operation Warp Speed and previous research into coronavirus vaccines, it still took the public and private sectors almost a year to produce viable vaccine candidates, and that timeframe was considered quick (as compared to vaccine development in non-crisis situations). While we take the time to develop and implement needed response measures, humans, animals, and plants fall ill and die.

LACK OF INVESTMENT

Having under-invested before biological events occur, we cannot respond quickly when these events arise. We also spend more money in the push to get what we need to contain the spread and impact of diseases than we would have had we paid in advance. Without sufficient investment, scientific efforts languish, promising programs grind to a halt, and technology advances slowly. Time and time again, we look back belatedly and bemoan our lack of consistent, committed investment. The short-term investments made in developing a vaccine for SARS (caused by SARS-CoV-1) and the decision to cease investing in these efforts before producing a vaccine certainly came back to haunt us during COVID-19.

LACK OF INNOVATION

While the United States values scientific breakthroughs and innovative technologies, we choose to rely on current options and justify purchasing them to bolster our preparedness without allowing for the possibility of better, more useful technologies over time. This problem is not unique to the biological arena. For example, despite innovations in communications technology production of fiber optic cables that could run underground, FEMA chose repeatedly to purchase poles and wire to replace telephone systems destroyed when hurricanes hit Hawaii. They did so because contracts to purchase them were already in place and the Agency knew that it could quickly reestablish communications by doing so.[180] It was not until Hawaii declined this federal support entirely that FEMA issued contracts for fiber optic cables to replace the antiquated system. Similarly, the world depends on archaic egg-based vaccines for the same reasons. Innovations are needed in science, technology, and bureaucracy.

LACK OF CAPABILITY AND CAPACITY

During non-emergency situations, current capabilities and capacities meet most needs and are rarely overwhelmed by ordinary events. However, those same capabilities and capacities proved inadequate during the responses to even small-scale biological incidents. The inability to scale up and expand manufacturing and other activities further exacerbates this problem.

LACK OF PREPAREDNESS

Preparedness costs money and is often viewed as an unnecessary expense in the absence of events requiring response. Yet when these events inevitably occur, the cost to respond is inversely proportional to investments in preparedness. From a business perspective (including the business of government), it makes sense to spend less overall by investing in preparedness–but only if we believe that events will occur that require responses. If we believe these events will not occur or occur so seldomly that someone else will respond, we will not invest in preparedness. National policy revolves around perceptions. Since we believe other nations may attack us, we support military preparedness activities and requirements. But even the military loses resources when times goes by without incident or attack. Similarly, support for public health drops to abysmally low levels because the profession successfully eliminates and controls so many diseases, injuries, and harmful behaviors that the public and funders no longer believe they will re-emerge or even continue to exist.

LACK OF QUICK RESPONSE CAPABILITY

For years, our country prided itself on its ability to respond to health crises. We still value this capability so much so that we optimize daily response activities (e.g., those undertaken by hospital emergency departments) at the expense of others (e.g., preventive screening). Without prevention, deterrence, surveillance, and detection, biological events affecting national security prove that the Nation is not able to respond quickly and that our initial response efforts are inadequate to meet the need. Large-scale events are particularly challenging. We need medical countermeasures, diagnostic tests, and data analysis immediately, but can rarely produce them quickly. Rapid response requires prior investment, preparedness, and implementation of mitigation efforts. It should come as no surprise that we cannot respond swiftly to biological events without prior investments in preparedness—but nevertheless, we are always surprised.

LACK OF ADEQUATE DATA

As with the Industrial Age, the Information Age emphasizes production (in this case, of data and information). Unfortunately, data quality varies radically, with even high- and low-quality data virtually indiscernible. Access to data also varies, so existing data may be inaccessible. Health care data and public health data systems are disjointed and usually unable to share information. These data-related issues prevent rapid alerts, accurate disease forecasts, understanding where and how epidemics grow into outbreaks (and by extension, epidemics and pandemics), and whether efforts to contain the spread of diseases are successful. Data and data-related inadequacies also impede surveillance and detection efforts.

LACK OF GOVERNANCE

For many years, it was considered either too difficult to address the biological threat, not a priority, or unnecessary to address separately from the chemical threat. High-level White House interest declined precipitously after President Richard Nixon shut down the US offensive biological weapons program in 1976. However, the biological threat never fully escaped White House attention. All presidential administrations since the Wilson Administration have dedicated at least a few staff to addressing pandemic influenza and biological weapons. Similarly, Congress has consistently paid some attention over the years, increasing and decreasing the number of congressional committees addressing the threat as biological events occurred and subsided. Regardless of the threat or severity of the threat, Congress and the White House continue to rush to overcome policy shortcomings and limited funding to help the United States respond when biological events occur. Our protracted experience in addressing COVID-19 proves this point. Without comprehensive governance adeptly knitting together the miscellaneous activities undertaken by all Cabinet agencies, eight independent agencies, and one independent institution, as well those executed by non-federal governments, academia, industry, and nongovernmental organizations, these weaknesses in biodefense will remain. It is only a matter of time before naturally occurring, accidentally released, or intentionally introduced pathogens and biological agents take advantage of these gaps and shortcomings and exploit the vulnerabilities they create.

CONCLUSION

We can meet and defeat the biological threat by embarking on The Apollo Program for Biodefense with its Athena Agenda. We have accomplished other grand projects in the past. By incorporating the success factors of previous impactful programs listed in Appendix B, we can ensure success.

APPENDIX B: HISTORICAL GRAND PROJECTS

Previously accomplished grand projects successfully accomplished their goals and objectives. We can learn from the factors that made them successful and apply them to The Apollo Program for Biodefense as well. A clearly defined mission, priorities, and goals serve as the foundation of any grand project. Strong leadership and support from the White House and Congress have also been essential to spur needed innovative research and development in the public and private sectors. Additionally, military involvement in, and international collaboration on, grand projects have been common success factors in the past. **From the Panama Canal in 1914 to Operation Warp Speed in 2021, the following factors led to the success of many grand projects:**

- **Clear mission, priorities, and goals**
- **White House leadership**
- **Congressional appropriations and support**
- **Innovative research and development**
- **Public-private partnerships**
- **Military involvement**
- **International collaboration**

Figure 6. Grand programs and the factors that led to their success.

1902–1914:
Panama Canal

Western powers have contemplated passage through the Panama Isthmus since the 16th century. For many years, American legislators considered whether to pursue a new project in Nicaragua or resume French efforts in Panama. Congress eventually put this debate to rest when it enacted the Spooner Act of 1902 (also referred to as the Panama Canal Act, 32 Stat. 481). President Theodore Roosevelt supported Panama's separation from Colombia and dealt directly with the Panamanian government since the Colombians rejected America's proposed financial terms for the project.

Top Priority:
To facilitate trade and expedite military travel between the Atlantic and Pacific Oceans

Budget:
$350–400 million (~$11 billion today)

Elements of Success:

- Clearly articulated mission, priorities, and goals
- White House leadership
- Congressional appropriations and support
- Military involvement and management
- Congressional funding
- Innovative research and development
- Private sector involvement
- Military involvement
- Understanding the failures of the French campaign
- Innovative architectural ideas
- Partnership with the Panamanian government

Continued

1941–1947:
Manhattan Project

This project enabled the United States to build a nuclear weapon and effectively determine the outcome of World War II. Furthermore, the existence of the bomb itself established the United States as the world's first superpower.

Top Priority:
To ensure the national security of the United States

Budget:
$2 billion (~$23 billion today)

Elements of Success:

- Clearly articulated mission, priorities, and goals
- White House leadership
- Congressional appropriations and support
- Innovative research and development
- Private sector involvement
- Military involvement
- Research contributions from the United Kingdom and Canada
- Wartime economy
- Access to natural resources in the United States

Continued

1956–1992:
National Highway System

The need for an interstate highway system reemerged after World War II and culminated in the National Interstate and Defense Highway Act of 1956 (also known as the National Interstate Act, P.L. 84-627). The American public supported President Dwight D. Eisenhower's plans for the system because they understood that efficient transportation was essential to their national defense and interstate commerce. Competent leadership established standardized features (e.g., use of odd numbers for north-south and even numbers for east-west interstates, uniform color scheme for signs, strategically placed access points).

Top Priority:
To prepare for a war fought on domestic soil

Budget:
$114 billion (~$500 billion today)

Elements of Success:

- Clearly articulated mission, priorities, and goals
- White House leadership
- Congressional appropriations and support
- Innovative research and development
- Private sector involvement
- Military involvement
- Clear and easy to understand standards
- Federal funding (as opposed to the previous system that relied heavily on state funds)
- Access to important natural resources
- Availability of models used by other countries

Continued

1961–1972:
Lunar Apollo Program

The Lunar Apollo Program was established to compete against the Former Soviet Union's progress in space. It is often assumed that the Apollo missions received a greenlight because Soviets had successfully launched Sputnik into space. While this certainly played a role in convincing Congress, President John F. Kennedy's self-perceived failure in the Bay of Pigs invasion combined with NASA's lack of progress prior to the Vostok I launch actually prompted executive approval. Kennedy later remarked that a US space program would be the "highest kind of national priority," thereby shifting attention from the Cold War in Latin America to the unlimited potential of space.

Top Priority:
To land on the Moon ahead of the Former Soviet Union

Budget:
$28 billion (~$280 billion today)

- Elements of Success:
- Clearly articulated mission, priorities, and goals
- White House leadership
- Congressional appropriations and support
- Innovative research and development
- Private sector involvement
- Military involvement
- Strong central leadership
- Engineering capabilities in the private sector
- Competition with the Former Soviet Union

Continued

1967–1979:
Smallpox Eradication

This program called for an international effort, and as such, the United States played an important leadership role by donating vaccines and appointing its own epidemiologists like Dr. Donald A. (D.A.) Henderson to positions of authority within the WHO. Accordingly, the last confirmed case of smallpox occurred in 1978 in the United Kingdom, the result of a laboratory accident.

Top Priority:
To eradicate smallpox

Budget:
$300 million (~$1.15 billion today)

Elements of Success:

- Clearly articulated mission, priorities, and goals
- White House leadership
- Congressional appropriations and support
- Innovative research and development
- Private sector involvement
- Military involvement
- International cooperation (with no resistance from countries in which smallpox was endemic on grounds of sovereignty)
- Decades of research

Continued

1973–2000:
Global Positioning System

The creation of our Global Positioning System (GPS) was a national security project that began in response to the Former Soviet Union's Sputnik launch. American scientists quickly deduced that they could pinpoint where a satellite was in orbit using the Doppler effect. Afterward, the US began testing inverse applications of that theory. The initial GPS technology served as the cornerstone for nuclear deterrence policy and as an offensive measure.

Top Priority:
To identify the location of enemy ships, aircrafts, and personnel

Budget:
$12 billion for initial construction; $2 million a day for maintenance (~$23 billion today)

Elements of Success:

- Clearly articulated mission, priorities, and goals
- White House leadership
- Congressional appropriations and support
- Innovative research and development
- Private sector involvement
- Military involvement
- Previous technological advancements
- Competition with the Former Soviet Union

Continued

1983–1998:
International Space Station

At a meeting on December 1, 1983, to discuss commerce and trade, NSC staffer Gil Rye and political strategist Craig L. Fuller stressed the benefits that the International Space Station (ISS) could bring to the US economy, specifically with regards to private sector growth. The primary goal of ISS research was to understand the effects of space on the human body and find solutions for extended space travel. In pursuing this research, NASA also discovered innovations that had everyday applications on Earth (e.g., scratch-resistant lenses, rubber molding used in shoes, polymer fabric used in firefighter suits, computer mouses, improvements to Lasik eye surgery).

Top Priority:
To develop a scientific laboratory, manufacturing and maintenance facility, and potential staging base for future space travel to the Moon, Mars, and other remote parts of the solar system

Budget:
$150 billion (~$255 billion today)

Elements of Success:

- Clearly articulated mission, priorities, and goals
- White House leadership
- Congressional appropriations and support
- Innovative research and development
- Private sector involvement
- Military involvement
- Academic involvement
- International collaboration

Continued

1990–2003:
Human Genome Project

The Human Genome Project (HGP) was a purely scientific endeavor that eventually yielded benefits for molecular medicine, mutation identification, and forensic science, as well as improved understanding of human evolution. Progress in forensic science expedited the identification of dangerous criminals. Private sector involvement also played a key role.

Top Priority:
To identify the base pairs that make up human DNA of its own volition

Budget:
$3 billion (~$6.1 billion today)

Elements of Success:

- Clearly articulated mission, priorities, and goals
- White House leadership
- Congressional appropriations and support
- Innovative research and development
- Private sector involvement
- International scientific and financial contributions

Continued

2020–2021:
Operation Warp Speed

For this project, the government partnered with the private sector to develop, approve, and distribute COVID-19 vaccines at an unprecedented pace. The decision to engage in this effort was due to the public health emergency created by COVID-19. National leadership mobilized as many resources as possible in an effort to create a vaccine.

Top Priority:
To develop vaccines for COVID-19

Budget:
$12.4 billion

Elements of Success:

- Clearly articulated mission, priorities, and goals
- White House leadership
- Congressional appropriations and support
- Innovative research and development
- Public-private partnerships
- Military involvement
- International collaboration
- Reduced bureaucracy that would otherwise slow down research

For more than 100 years, these success factors have been common to nearly every grand program or project undertaken by the United States. The Apollo Program for Biodefense will have the best opportunity to succeed if it incorporates these elements. The Program will require a clear mission with set priorities and milestones for achieving goals. Success will also require White House leadership and adequate, sustained funding from Congress. Public-private partnerships will be necessary to harness innovative technology developments and bring them to fruition. As demonstrated with Operation Warp Speed, the Program will also need military involvement to provide logistics and support. Finally, success will require international collaboration because biological threats do not respect borders. History repeatedly demonstrates that if we incorporate these factors, we can successfully accomplish previously unimaginable feats.

The following sections provide insight into the personal and political triggers that drove important decisions and mistakes made during the execution of these projects.

NATIONAL PRIORITIES

Grand historical projects in the United States are justified consistently on the grounds of three distinct priorities: (1) national security, (2) the economy, and (3) public health or science. This order is hierarchical and supported by the frequency, funding, and time allocated by the government. Additionally, these factors are widely articulated in the legislative records, administrative correspondences, and biographies of leading political figures.

The President of the United States has a direct line to the American people, and as such, can influence legislative decisions by galvanizing society at large. Alternatively, in the absence of Congressional approval, there may enough federal funding available at the President's discretion to implement at least some recommendations from The Apollo Program for Biodefense by extension, Cabinet members and those in charge of federal departments and agencies also have tremendous influence.[181]

Support can also be acquired by emphasizing unforeseen or lesser-known outcomes that might occur because of residual effects from grand projects. Take for instance construction of the Panama Canal. At face value, connecting the Atlantic and Pacific oceans had predictable upsides for international trade. However, when the Canal underwent expansions in 2016, this set a new design standard for cargo ships (respectively called the Neo-Panamax) and forced US cities to make architectural changes to their ports, thus leading to the creation of trans-shipment hubs and a new multi-billion-dollar industry; all of which were not predictable at the time the decision to expand was made.[182,183,184]

The United States has benefited from NASA's research on the ISS in a variety of unanticipated ways. The primary goal of ISS research was to understand the effects of space on the human body and find solutions for extended space travel; but in doing so, NASA discovered innovations that had an application in everyday life. Among these discoveries include the development of scratch-resistant lenses, rubber molding used in athletic sneakers, polymer fabric used in firefighter suits, computer mouses, and improvements to Lasik eye surgery.[185,186]

First and foremost, The Apollo Program for Biodefense addresses significant and immediate national security concerns. Wars are a cyclical trend in the modern world and can manifest as all-out conflicts, proxy wars, or even decisions on economic policy. Given that peace is elusive to those with an interest in the affairs of others, the United States has not been an exception to this rule since its emergence as a superpower, whereupon it fully embraced interventionist policies. Nevertheless, with every conflict, the opportunity for drastic, if not radical change, always presents itself. National security is a topic that will never go away; it is etched into the forefront of every policymaker's mind regardless of party allegiance.

For over a century, national security concerns have dictated American political discourse. Under President Woodrow Wilson, the United States abandoned its long-held isolationist views to become a major player in global affairs. Following the next three decades of turmoil, which featured both world wars and growing anti-colonial sentiments in developing countries, traditional Western powers like the United Kingdom, France, and Germany, could no longer vie for superpower status, and as a result, only the United States and Soviet Union remained as contenders. In turn, this set the stage for the Cold War that would dominate US policy for the next 50 years.

As such, many of the grand historical projects implemented were rationalized by a need to contain Soviet influence in the developing world. For example, despite appearing as largely scientific endeavors, both the ISS and original Apollo Program were conceived as countermeasures to the Soviet Union's progress. With respect to Apollo, it is often assumed that the mission received a greenlight because Soviets had successfully launched Sputnik into space. While this certainly played a role in convincing Congress, it was not the proverbial straw that broke the White House's back. Ultimately, it was President John F. Kennedy's self-perceived failure in the Bay of Pigs invasion combined with NASA's lack of progress prior to the Vostok I launch that prompted executive action.[187,188] Kennedy later remarked that a US space program would be the "highest kind of national priority," thereby shifting attention in the Cold War from Latin America to the unlimited potential of space.

In contrast, US research in space is conducted from the ISS. At the time of its conception in 1984, the ISS was intended for exclusive use by the United States, to strengthen US military prowess, and promote economic growth. A year earlier, Reagan had also introduced plans for the Strategic Defense Initiative, a missile defense system that could shoot down

intercontinental ballistic missiles from space, thereby eliminating the threat of nuclear war for good. Both ultimately failed and plans to build the space station evolved into an international project between five independent agencies, which ironically included the reformed Soviet Union state of Russia and excluded China.

Current tensions between the US and China are reaching new heights.[189,190] As a result, China portrayed themselves to the world as a leader in global health, which in turn has major implications for our national security.

For nearly 50 years, decisions regarding US activity in space were motivated by fears that the Soviet Union would exceed American technological capabilities or perceived by the rest of the world as such. The same logic should apply to our present need for a robust and thorough biodefense program. The purpose of The Apollo Program for Biodefense is not to encourage an arms race, but rather keep Americans, and by extension the rest of humanity, safe from future pandemics. Given our understanding of the original Apollo mission and construction of the ISS, The Apollo Program for Biodefense should succeed as a national security measure not only by protecting the US against biological threats, but also by rebuilding American status in the international community as a nation that can keep its own people safe.

In addition to the space program, the United States also enacted two other large national security projects during the Cold War era: construction of the national highway system between 1956 and 1992, and creation of GPS technology in 1973. Under President Dwight D. Eisenhower, the nation took significant strides to improve domestic infrastructure as a means for ensuring the US military could navigate within America if attacked.[191,192]

The creation of our GPS was also a national security program that began in response to the Soviet Union's Sputnik launch. American scientists discovered that they could pinpoint where a satellite was in orbit using the Doppler effect. Shortly thereafter, the US began testing inverse applications of that capability to develop GPS. The initial GPS technology served dual functions: first, as a cornerstone for nuclear deterrence policy, and second, as an offensive measure to identify the location of enemy ships, aircrafts and perhaps, even individual soldiers.[193] These priorities changed in 1983 when a Soviet interceptor shot down a Korean passenger jet that had strayed from its intended route and into prohibited airspace. With an understanding that GPS could have prevented this incident, the Reagan Administration made it available for civilian use with the caveat that they would jam some signals to preserve US military tactical advantages.[194,195]

Furthermore, the American tradition of promptly responding to national security threats by authorizing grand projects dates to before the Cold War, as exemplified by the Manhattan Project. President Franklin D. Roosevelt's decision to begin work on a nuclear weapon was motivated primarily out of fear that Germany would have a decisive advantage in World War II and thus, consolidate its control over all of Europe. At the time, the United States took a

neutral position in the conflict; but secretly, it had begun preparing for a number of different outcomes. Ultimately, the Manhattan Project was a success and it resulted in the creation of the world's first atomic bomb. This in turn secured Allied victory in World War II by forcing Japan to surrender after the bombings of Hiroshima and Nagasaki. Likewise, The Apollo Program for Biodefense can pacify risks posed by biological threats through deterrence by denial,[196] which transcends beyond the capabilities of rival nations, terrorist networks, and specific individuals, to nature itself.

The Apollo Program for Biodefense would yield unprecedented economic benefits that ensure a healthy, functioning labor force, have the potential to create jobs, and protect the current and future integrity of the US economy. After national security, the economy reigns supreme on the extensive list of national priorities. People typically vote based on how their bottom line is affected; namely factors spanning from taxes and employment to quality of life and access to resources. As such, most grand historical projects had significant economic implications. Projects like the national highway system and GPS, while decided on the grounds of national security, both had foreseeable and unforeseeable economic benefits. Additionally, public health programs have an inherent effect on the economy because the most valuable resource in any nation is the health and well-being of its citizens and workforce. Since the United States is currently recovering from a recession that spurred on by COVID-19, many Americans are eager to see improvements to the economy.

Despite the Panama Canal finalizing construction efforts just days before the start of World War I and allowing US naval forces to support war efforts in both the Pacific and Atlantic theaters during World War II, this grand project was primarily driven by the desire to facilitate international trade. Its origin dates back as early as the 16th century when several European nations contemplated undertaking construction efforts on the Panamanian isthmus. Americans were sold on the idea as early as 1788, when Thomas Jefferson approached Spain to build a canal in one of its colonies. However, it wasn't until 1902 that the US finally embarked on its mission to construct a canal after taking the reins from France who had previously spent 13 years trying to build one.[197,198]

The Panama Canal remains one of the only historical grand projects primarily advanced as an economic policy. The ideologies surrounding western expansion, combined with the Industrial Revolution and rise of US global influence, resulted in concerns over the speed of international trade. By constructing the Canal, the US not only eased burdens on the shipping industry for itself, but it also inherited a way to generate profit from foreign countries. Though France had failed miserably in its campaign—which left over 22,000 workers dead and $280 million wasted—the United States remained undeterred and pressed onward, all for the sake of economic growth. To that end, Americans lent support to Panamanian independence from Nicaragua in exchange for the opportunity to construct and operate a canal on their soil.[199,200,201]

Many of the efforts that were conceived for national security reasons also had economic implications. Both Apollo and the ISS led to the creation of new technologies for use in everyday life and provided private sector opportunities for engineering companies like Boeing. The Manhattan Project, which was established strictly as a war effort, created jobs for nearly 120,000 Americans at a time when overall employment was low. And as previously touched upon, the national highway system and creation of GPS yielded exponential benefits for domestic travel, which ultimately led to a wider range of job opportunities and market spending for the public.

In addition to causing a recession, COVID-19 has completely altered conventional aspects of the US economy by unveiling which jobs or industries are expendable, disrupting the flow of education, exacerbating the spread of dis- and misinformation, and creating a work from home environment. Future pandemics have the potential to collapse national economies in their entirety.

The Apollo Program for Biodefense has the public health benefit of imbuing the United States with the capability to prevent future pandemics and eliminate catastrophic biological threats to humanity's long-term survival. Public health is an important priority for the government as exemplified by the eradication of smallpox during the 1970s following a global vaccination campaign led by WHO. The program called for an international effort, and as such, the United States played an important leadership role by donating vaccines and appointing its own epidemiologists like Donald Henderson to positions of authority within WHO.[202] Accordingly, the last confirmed case of smallpox was recorded in 1978 in the United Kingdom, resulting from a lab accident.[203] Unfortunately, since both the United States and the Soviet Union continue to have access to smallpox samples, it still poses a viable threat to society. Furthermore, advancements in biotechnology now allow individuals with the proper knowledge to replicate smallpox in laboratories.

In 1990, the United States initiated the HGP with the primary goal of determining the base pairs that make up human DNA. Originally planned by the Reagan Administration, the HGP was a purely scientific endeavor that eventually yielded benefits for molecular medicine, identifying mutations, forensic science, and understanding human evolution. Additionally, progress in forensic science had national security implications by expediting the discovery and interception of individuals who pose a danger to the public.[204]

Lastly, and most recently, the Trump Administration enacted Operation Warp Speed to develop vaccines for COVID-19. This project enabled the government to partner with the private sector to develop, approve, and distribute COVID-19 vaccines at an unprecedented pace. Ultimately, this decision was a public health necessity made in response to the enormous impact of COVID-19. At the time of its approval, the United States was on track to reach 100,000 deaths, which would have been more than the total number of war-related deaths since 1975.[205,206] This may sound relatively inconsequential today, given that we have already exceeded a death toll of about one million people.

Economic factors played a role in this decision as well. During the second fiscal quarter of 2020, GDP growth in the US fell by an astounding 31.4%, while unemployment rose to its highest rate since World War II at roughly 14.7%.[207] For the Americans who continued to have jobs, millions were still placed on furlough, and several signature industries of the US economy like leisure, service, and travel were left in complete disarray.

The government initiated the eradication of smallpox and Operation Warp Speed because allowing hundreds of thousands of people to die would have been politically disastrous and ethically wrong. Failing to implement proactive measures that can prevent future pandemics is likewise immoral. The further we move away from 2020, the less urgency we have on our side. Even though smallpox did not suddenly spike in the 1970s, US foreign policy still gravitated towards more involvement with other countries, and as such, the necessity to address the disease began to mount in the minds of our national leaders. Overall, these examples set a precedent for enacting ambitious, large-scale science and public health programs.

LOGISTICAL MANAGEMENT

Success depends on consistent leadership and adequate funding ensured over a lengthy period. Adequate funding over a lengthy period has played a vital role in the success of nearly every grand historical project. Funding approved by Congress and earmarked for specific projects provides buffer room for experimentation and error in the early stages of a project, which often proves vital in the long run. On the other hand, funds that are available for the President to use at his or her discretion can run afoul of several issues like limited time for research and preparation, opinion shifts within an administration, or even complete administration changes after a new election cycle.

When Congress approved the national highway system, they restructured funding through the National Interstate Act that directed the government to pay 90% of the costs of construction. Prior to this, states were responsible for 50%, a percentage many opined to be unfair and in violation of the federalist principles long held within the United States. As a result, the government was able to commandeer interstate resources and labor at an expeditious rate, which ultimately led to the domestic travel system we enjoy today.[208] Furthermore, the government continues to maintain and repair national highways with funding appropriated by Congress.

Similarly, the creation and maintenance of the GPS system requires a continuous stream of funding. The initial construction cost of GPS satellites is estimated around $12 billion and US taxpayers continue to spend approximately $2 million a day for maintenance. These expenses are justified by the widespread use and application of GPS in everyday life.

On the other hand, original plans for a space station exemplify what happens when funding is not secured over an extended period of time. The US initially sought to control

a space station exclusively. However, after Congress refused to front a larger bill, the Clinton Administration had to salvage plans by striking a deal with outside space agencies, thereby splitting ownership and control over the station. The ISS has since been operated concurrently by five distinct space agencies that collectively represent fifteen nations: NASA (United States), Roscosmos (Russia), JAX (Japan), CSA (Canada), and ESA (Europe).[209] Although these agreements secured the requisite funding and ultimately provided the United States with the ability to regularly conduct science experiments from space, they also restrict Americans from being able to prevent outside access and fulfill clandestine objectives, which were certainly among the original priorities for having a station in the first place.

While implementing The Apollo Program for Biodefense, the Executive Branch should seek out international partnerships and incentivize the private sector to play a role in advancing technology. As previously touched upon with the ISS, international partnerships can prove effective when there is lack of Congressional support at home. However, it is more ideal for the United States to retain its independence and seek out partnerships that result in the sharing of ideas rather than in equal control over projects. The best example of this occurred during construction of the Panama Canal. Under the French campaign that lasted from 1881 to 1894, operations were directed at the helm of Ferdinand de Lesseps who had previously found success in constructing the Suez Canal.[210] However, de Lesseps severely underestimated weather conditions in Panama and dismissed alternative design proposals like those suggested by Philippe Bunau-Varilla.[211] Ultimately, this contributed to France's failure, of which American leaders subsequently acknowledged and took precautions to avoid repeating the same mistakes. Unlike de Lesseps, American military leaders who oversaw construction embraced the novel ideas set forth by Bunau-Varilla and were able to succeed.[212]

In addition to seeking out international partners, collaborating with the private sector can boost innovation, as shown by Operation Warp Speed. In 2020, the government successfully incentivized participation from private companies to develop a COVID-19 vaccine. This directly led to the creation of Moderna's vaccine, as they were one of eight private corporations who received funding.

Similarly, NASA now contracts with private companies like SpaceX, who in recent years has sent new modules and improvements to the ISS, as the trend of private exploration continues to rise.[213] Private sector involvement also played a key role during the HGP. A private company was able to capitalize on the data made available by the project and apply for patents on thousands of genes. Additionally, projects like the Brain Research through Advancing Innovative Neurotechnologies (known as BRAIN) Initiative, the National Nanotechnology Initiative, and the Advanced Research Projects Agency Network (known as ARPANET) that created a technological foundation for the internet, all relied on executive funding provided to private research institutions and companies to achieve their intended goals.

CONCLUSION

Historical grand projects give us an understanding of how national priorities are consistently determined. The best course for implementing The Apollo Program for Biodefense begins with the Executive Branch because the President can speak directly to the people and inspire a collective call to action. History also reveals that larger programs tend to carry a number of unpredictable positive residual effects. Furthermore, grand historical projects provide lessons on how The Apollo Program for Biodefense can be effectively implemented. This includes securing Congressional funding for an extended period because discretionary funds available to the Executive Branch can run afoul of rapid priority changes.

The Apollo Program for Biodefense will take several years to fully blossom, and some technologies and capabilities will take more time to develop than others. However, implementing these recommendations should be the highest priority given our current experience with the COVID-19 pandemic. US leaders should seek out international partners and induce competition in the private sector to ensure that we consider all possible alternatives and expedite the rate of innovation.

In conclusion, The Apollo Program for Biodefense requires an all-hands-on-deck approach to effectively address the national security, economic, and public health issues looming over current US biodefense policy or lack thereof. We have an opportunity to change the course of history and enact measures to prevent the occurrence of future pandemics. There is no greater calling than to ensure the survival of our species.

History also reveals that larger programs tend to carry a number of unpredictable positive residual effects.

APPENDIX C: METHODOLOGY

The Bipartisan Commission on Biodefense was established in 2014 to inform US biodefense and provide recommendations for change. The Commission, supported by academia, foundations, and industry, determines where the United States falls short in addressing bioterrorism, biological warfare, and emerging and reemerging infectious diseases.

RESEARCH QUESTIONS

To develop The Apollo Program for Biodefense, we developed the following research questions.

Technology Priorities and Needed Capabilities

- What should be the top priorities for an Apollo Program for Biodefense?
- Are investments in the development of technologies commensurate with the challenge of biodefense?
- Is new funding required?
- What should we be doing that we are not already doing to address biological threats more adequately with technology?
- How will the biological threat landscape evolve over the next decade and what technologies are needed to ensure preparedness?
- How can the public and private sectors contribute to an Apollo Program for Biodefense?
- How can we be sure that new technologies for biodefense have limited dual-use potential?

- How will technological convergence shape the biological threat landscape moving forward? What should be taken into consideration?
- What sorts of policy initiatives could drive technological innovation for biodefense on the scale of an Apollo program?

Historical Grand Projects: Aspects of Successful Models

- How did national leadership decide on the top priority for each of these programs?
- What elements of the constructs for these programs made them successful?
- What high-impact outcomes resulted and how were they connected to these elements?
- How did industry, academia, the military, and civilian government work together to form alliances and other public-private partnerships for overall program success?
- What roles did the Administration, White House staff, and Congress play in leadership, management, administration, communication, authorization, and appropriations?
- How were scientists identified, chosen, recruited, and included in these programs?
- How did the military lead, participate in, or otherwise engage in these programs?
- How did these programs contribute to or affect national security?

How These Aspects Could be Applied to an Apollo Program for Biodefense

- What should be the top priority for this Program?
- Should the top or first priority for the Program be the development and production of a universal influenza vaccine?
- What should be the elements of a new construct for biodefense?
- What specific extremely high-impact outcomes could result?
- How can the government, academia, and corporate America contribute?
- How best should the Administration lead this Program? What specific actions should the White House take to bring the program to fruition?
- How best should Congress support this Program? What specific actions should Congress take to bring the project to fruition?
- Which leading scientists should play a significant role in the Program?
- What role should the military play in leading, coordinating, or managing this Program?
- What are the implications of the Program for national security?

PRELIMINARY RESEARCH

The Commission reviewed previous research efforts; scientific studies; previous US government research and development programs; and federal strategies, plans, funding, and research and development programs related to defense against naturally occurring, accidentally released, and intentionally introduced biological threats and catastrophic biological risks. This review allowed for an assessment of the comprehensiveness and effectiveness of research and development efforts for biodefense; and determined direction for an Apollo Program for Biodefense. This review also informed the structure and topics of a formal meeting of the Commission, and interviews and roundtables with subject matter and government experts.

FORMAL MEETINGS

During three formal meetings to address and inform a grand project for biodefense, Commissioners, ex officio members, and staff received (1) information regarding current relevant national policy, legislative issues, and departmental and agency programmatic activities; and (2) statements from current and former Members of Congress, current and former federal officials, state, and local representatives, thought leaders, and subject matter experts. Commission staff summarized the major insights, areas for improvement, and recommendations articulated by meeting speakers, and conducted preliminary high-level analysis of each day-long meeting.

INTERVIEWS OF EXPERTS

The Commission conducted interviews with 66 academic, industry, non-governmental, and governmental experts to inform the recommendations contained in this report. Experts were invited to participate based on their prior knowledge of and experience with public health security, technological development, biosecurity, and biodefense. Staff protected the privacy of each expert to speak openly and candidly, and did not attribute opinions to the institutions, organizations, agencies, departments, or employers with which they were affiliated. Opinions were considered on aggregate. This report contains the views of the Commission and not necessarily those of individual experts.

ROUNDTABLES

The Commission hosted four roundtables at which experts discussed challenges and solutions that an Apollo Program for Biodefense should address in the following areas:

- Innovative pathogen biosurveillance
- Improved PPE and built environments that prevent the transmission of disease
- Advanced medical countermeasures to combat biological threats
- Improved microbial forensics and attribution

The Commission held these roundtables using virtual platforms in September 2020. Participants came from a diverse range of backgrounds, including academia, industry, non-governmental organizations, and government. To encourage frank and open discussion, the Commission held these roundtables under Chatham House Rule. Staff provided questions to participants in advance. During these roundtables, participants discussed ambitious proposals and solutions for a wide range of biological threats.

ANALYSIS

Commission staff used qualitative methods to analyze information and data obtained during the literature review, meetings, interviews, and roundtables. Staff examined the oral statements provided by meeting speakers. Staff synthesized and evaluated ideas, feedback, and suggestions to help inform the development of the Athena Agenda to execute The Apollo Program for Biodefense. Staff further evaluated findings and recommendations with additional policy research and interviews with subject matter experts and former high-level government officials, as well as in light of the Commissioners' own experiences. Throughout the process, the research questions defined previously provided the basis for assessment. Staff did not use statistical and other quantitative methods for this analysis.

LIMITATIONS

Several biodefense programs and policies; intelligence, raw data, and documents; appropriations and budget documents; and other sensitive information are classified or otherwise unavailable and, accordingly, were not reviewed by the Commission.

APPENDIX D: MEETING AGENDAS

A MANHATTAN PROJECT FOR BIODEFENSE: TAKING BIOLOGICAL THREATS OFF THE TABLE

July 11, 2019
58 E 68th St, New York, NY 10065

OBJECTIVE
Inform Panel deliberations on how best to create a national, public-private research and development undertaking to defend the United States against biological threats.

SCHEDULE

9:00 – 9:15 am Opening Remarks

9:15 – 10:15 am
Panel One – Case Study: Pursuit of Universal Influenza Vaccine Federal and military officials, and an academic representative, discuss efforts to develop universal influenza vaccine, the challenges associated with science and funding, arguments for and against such an approach, and what it will take to get it across the finish line.

Alan Embry, PhD
Chief, Respiratory Diseases Branch, National Institute of Allergy and Infectious Diseases, National Institutes of Health

Blake Bextine, PhD, MA
Acting Deputy Director, Biological Technologies Office, Defense Advanced Research Projects Agency

Ren Sun, PhD
Distinguished Professor, Molecular & Medical Pharmacology and Bioengineering; Associate Dean for Postdoctoral Affairs, David Geffen School of Medicine; Associate Vice Provost for Internationalization, University of California Los Angeles

10:15 – 11:15 am Panel Two – Local View on Biological Threats and Requirements
Representatives from the New York City departments of police, health and transit discuss the biological threat from their perspective, what they need to defend against it, challenges in interacting with the federal government to achieve adequate biodefense of New York City, and requirements they believe a Manhattan Project for Biodefense should be addressed.

John O'Connell
Deputy Chief and Commanding Officer of the Counterterrorism Division, New York City Police Department

Beth Maldin Morgenthau, MPH
Deputy Commissioner, New York City Department of Health and Mental Hygiene

Michael Gemelli
Manager, Environmental Monitoring and Emergency Response, Counterterrorism and Security Initiatives, New York City Transit, Department of Security

11:15 – 11:30 am Break

11:30 – 12:30 pm Panel Three – Federal and Military Contributions
Representatives from federal and military agencies discuss cutting edge biodefense research, challenges associated with this research, and requirements for what they would consider a Manhattan Project for Biodefense.

Robert P. Kadlec, MD, MTM&H, MS (Colonel US Air Force – Retired)
Assistant Secretary for Preparedness and Response, US Department of Health and Human Services

Deydre S. Teyhen, PhD, DPT, OCS (Colonel US Army)
Commander, Walter Reed Army Institute of Research, Medical Research and Materiel Command, US Army

12:30 – 1:00 pm Break

1:00 – 1:45 pm Luncheon Keynote – Graphic History of Germ Warfare
Scholar and New York Times best-selling author provides historical perspective on biological warfare and bioterrorism, discusses the need for a Manhattan Project for Biodefense, and addresses the value of pop culture as a tool to educate and inform the public, government, and the private sector.

Max Brooks
Nonresident Fellow, Modern War Institute at West Point; Nonresident Fellow, Brent Scowcroft Center for Strategy and Security, Atlantic Council; Author, World War Z, The Zombie Survival Guide, The Harlem Hellfighters, and Germ Warfare: A Very Graphic History

1:45 – 2:00 pm Break

2:00 – 3:15 pm Panel Four – Non-Federal Contributions
Private sector representatives discuss needs, resource requirements, and business risks associated with their research contributions to the national biodefense enterprise and potential contributions to a Manhattan Project for Biodefense.

Monique K. Mansoura, PhD, MBA
Executive Director, Global Health Security and Biotechnology, The MITRE Corporation

Patricia Falcone, PhD, MS
Deputy Director for Science and Technology, Lawrence Livermore National Laboratory

Akhila Kosaraju, MD
President and Co-Founder, Variant Bio; former Vice President for Global Development, SIGA Technologies; former Special Assistant to the Assistant Secretary of Defense for Health Affairs, Department of Defense

3:15 – 3:30 pm Closing Remarks and Adjourn

THE BIOLOGICAL EVENT HORIZON: NO RETURN OR TOTAL RESILIENCE

September 24, 2020
(Virtual)

OBJECTIVE

Provide the Bipartisan Commission on Biodefense with a better understanding of emerging biological threats and innovative technology for biodefense.

SCHEDULE

9:00 – 9:30 am Opening Remarks

9:30 – 10:25 am Panel One: Congressional Perspective
Sitting Members of Congress discuss the role of the Legislative Branch in addressing biological threats.

Representative Susan Brooks (R-IN)
Member, Subcommittee on Health, Committee on Energy and Commerce, US House of Representatives

Representative Diana DeGette (D-CO)
Chair, Subcommittee on Oversight and Investigation, Committee on Energy and Commerce, US House of Representatives

10:25 am – 11:40 am Panel Two: Emerging Biological Risks
Academic and non-governmental representatives discuss emerging biotechnological risks and how biological threats like COVID-19 are becoming increasingly common.

Jaime Yassif, PhD
Senior Fellow, Global Biological Policy and Programs, Nuclear Threat Initiative

Sohini Ramachandran, PhD
Associate Professor of Biology, Director of Graduate Studies for the Center for Computational Molecular Biology, Associate Professor of Computer Science, Brown University

Nita Madhav, MSPH
Chief Executive Officer, President, and Board Member, Metabiota

11:40 am – 12:40 pm Panel Three: The Future of Biodefense
A non-governmental representative and a former federal official discuss emerging technologies and ways to improve federal efforts to harness this new technology for biodefense.

Kavita M. Berger, PhD
Director, Board on Life Sciences, National Academies of Sciences

Luciana Borio, MD
Vice President, Technical Staff, In-Q-Tel; Former Director for Medical and Biodefense Preparedness, Food and Drug Administration

12:40 – 12:45 pm Closing Remarks and Adjourn

THE ATHENA AGENDA: EXECUTING THE APOLLO PROGRAM FOR BIODEFENSE

December 8, 2021
1201 Pennsylvania Avenue, NW, Suite 400, Washington, DC 20004

OBJECTIVE

Provide the Bipartisan Commission on Biodefense with a better understanding of: (1) ongoing federal efforts to implement The Apollo Program for Biodefense; (2) the role of the private sector in implementing The Apollo Program for Biodefense; and (3) how the public and private sectors can fully implement The Apollo Program for Biodefense by the end of the decade.

SCHEDULE

10:00 – 10:30 am Opening Remarks

10:30 am – 11:15 pm
Panel Two: Executive Perspective
A government official discusses the role of the Executive Branch in ensuring that the public and private sectors work together to achieve The Apollo Program for Biodefense by the end of the decade.

> **Eric S. Lander, DPhil**
> Science Advisor to the President; Director, Office of Science and Technology Policy

11:15 am – 12:00 pm
Panel One: Congressional Perspective
A Member of Congress provide their views about the role of the Legislative Branch in implementing The Apollo Program for Biodefense.

> **Senator Richard Burr (R-NC)**
> Ranking Member, Committee on Health, Education, Labor and Pensions, and Chair, Subcommittee on Labor, US Senate

12:00 pm – 12:45 pm
Lunch and Video

12:45 – 1:50 pm

Panel Three: A Vision for Something Greater

Experts discuss their visions for what The Apollo Program for Biodefense could look like and how the public and private sectors can work together to achieve that goal.

The Honorable Tara O'Toole, MD, MPH
Executive Vice President, In-Q-Tel; former Under Secretary for Science and Technology, Department of Homeland Security

Jacob L. Swett, DPhil
Co-founder, altLabs; Visiting Scientist, Biodesign Institute, Arizona State University

Syra Madad, DHSc
Senior Director, System-wide Special Pathogens Program, New York City Health + Hospitals

1:50 – 2:55 pm

Panel Four: Coordinating Efforts and Strategic Direction

Two current and one former government official discuss the role of the federal government in achieving The Apollo Program for Biodefense by the end of the decade.

Stephen M. Hahn, MD
Chief Medical Officer, Preemptive Medicine and Health Security Initiative, Flagship Pioneering; Former Commissioner, US Food and Drug Administration

Sandeep Patel, PhD
Director, Division of Research, Innovation, and Ventures (DRIVe), Biomedical Advanced Research and Development Authority, US Department of Health and Human Services

Brandi C. Vann, PhD
Deputy Assistant Secretary of Defense for Chemical and Biological Defense Programs, US Department of Defense

2:55 – 3:10 pm *Break*

3:10 pm – 4:15 pm

Panel Five: Fostering Innovation at Scale

Experts discuss the role of the private sector and academia in achieving The Apollo Program for Biodefense by the end of the decade.

May Chu, PhD
Clinical Professor, Department of Epidemiology, Colorado School of Public Health; former Assistant Director of Public Health, Office of Science and Technology Policy; Executive Office of the President (Obama); former Director, Diagnostic Reference Laboratory for Bacterial Zoonotic Diseases, Centers for Disease Control and Prevention

Akhila Kosaraju, MD
CEO and President, Phare Bio; former Special Assistant to the Assistant Secretary of Defense for Health Affairs, US Department of Defense

Dan Wattendorf, MD
Director, Innovative Technology Solutions, Bill & Melinda Gates Foundation

4:15 – 4:30 pm Closing Remarks and Adjourn

GLOSSARY

Artificial Intelligence
The theory and development of computer systems able to perform tasks that normally require human intelligence.

Built environment
Human-made environments (e.g., offices, healthcare facilities, schools, public transportation, planes) where transmission of most known pathogens occur.

CRISPR
Clustered Regularly Interspaced Short Palindromic Repeat.

CRISPR-Cas9
Clustered Regularly Interspaced Short Palindromic Repeat, Associated Protein 9.

COVID-19
Coronavirus disease 2019.

Cyberology
The science, study, and theory of cyberspace and cybernetics, including communications over computer networks, Internet-connected systems and data centers, computerized systems, communications, and automatic control systems in both machines and living things.

Digital biomarkers
Detectable physiological, biometric, biophysical, biochemical, mobility, and circadian rhythm changes that occur when a pathogen infects the body.

Digital pathogen surveillance
Systems that use internet-based and other electronically available data (e.g., medical bulletins, search queries, social media) to provide real-time warning of infectious disease events.

DNA
Deoxyribonucleic acid.

DNA synthesis screening
Computer algorithms that scan commercial DNA synthesis orders for potential harmful biological agents.

Host-responses
The genetic and biological signs an individual produces when infected with a pathogen.

Immunogenicity
The ability of a foreign substance to provoke an immune response.

Inhalable administration
The delivery of a therapeutic or vaccine to an individual by breathing it into their lungs.

Intranasal administration
The delivery of a therapeutic or vaccine to an individual by spraying it in their nose.

Machine learning
The use and development of computer systems that can learn and adapt without following explicit instructions to analyze and draw inferences from patterns in data.

Massively multiplexed detection
Detection capabilities that can test for multiple pathogens, resistance genes, biomarkers, and analytes in a single simple assay.

Metagenomic sequencing
The reading of all genetic material from a sample.

Microfluidics
Instruments that use small amounts of liquid on a microchip to do laboratory tests.

Minimally- and non-invasive infection detection
Detection and diagnostic methods that permit sample acquisition, data collection, or early warning without pain, discomfort, inconvenience, or risk.

Monoclonal antibodies
Laboratory-produced molecules that act as substitute antibodies that can restore, enhance, or mimic the immune system's attack on cells.

mRNA
Messenger RNA.

Multi-pathogen therapeutic drugs
Also known as broad-spectrum therapeutics, these are drugs that can be effective against a wide variety of pathogens.

Multiplexed PCR assays
PCR tests that can identify approximately 25 of the pathogens most associated with respiratory infections, but do not include most known or novel pathogens.

Needle-free administration
The delivery of therapeutics and vaccines that are pain-free, cause minimal discomfort, convenient, and easy to distribute at scale.

Nucleic-acid sequencing
The reading of genetic material.

Oral administration
The delivery of a therapeutic or vaccine to an individual by ingesting it.

Pharmacokinetics
The study of the bodily absorption, distribution, metabolism, and excretion of drugs.

Platform technologies
Technologies that use the same processes for manufacturing, formulation, and delivery of a drug or vaccine against multiple different pathogens.

Rapid point-of-use diagnostics
Also known as point-of-person or point-of-need diagnostics, these are tests that can rapidly identify an infection wherever the individual is located.

RNA
Ribonucleic acid.

Prototype pathogen
A pathogen from a viral family that is used to develop platform vaccines or therapeutics for all pathogens in that family.

Sequence homology
The ability to detect similar regions in a pathogen's genetic tree.

SARS
Severe acute respiratory syndrome.

SARS-CoV-1
Severe acute respiratory syndrome-coronavirus-1.

SARS-CoV-2
Severe acute respiratory syndrome-coronavirus-2.

Transdermal administration
The delivery of a therapeutic or vaccine to an individual through their skin.

Ubiquitous sequencing
The routine use of sequencing in clinical and environmental settings that would result in a baseline understanding of the genetic material around us, permitting the early detection of new threats, while providing the critical diagnostic capacity needed to reduce the global infectious disease burden.

Volatolomics
The detection of volatile compounds emitted by an individual.

ACRONYMS

AI	Artificial Intelligence
ASPR	Assistant Secretary for Preparedness and Response
BARDA	Biomedical Advanced Research and Development Authority
BSL-4	Biosafety Level Four
CDC	Centers for Disease Control and Prevention
CIADM	Centers for Innovation in Advanced Development and Manufacturing
DARPA	Defense Advanced Research Projects Agency
DHS	Department of Homeland Security
DNI	Director of National Intelligence
DOC	Department of Commerce
DOD	Department of Defense
DOE	Department of Energy
DOI	Department of the Interior
DOL	Department of Labor
DOS	Department of State
DOT	Department of Transportation
ED	Department of Education
DRIVe	Division of Research, Innovation, and Ventures
FDA	Food and Drug Administration
FEMA	Federal Emergency Management Agency
GPS	Global Positioning System
GSA	General Services Administration
HGP	Human Genome Project
HHS	Department of Health and Human Services
IC	Intelligence Community
IGSC	International Gene Synthesis Consortium
ISS	International Space Station
NASA	National Aeronautics and Space Administration
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NSABB	National Science Advisory Board for Biosecurity
NSC	National Security Council

Continued

NSF	National Science Foundation
OMB	Office of Management and Budget
OSTP	Office of Science and Technology Policy
PPE	Personal protective equipment
RADx	NIH Rapid Acceleration of Diagnostics
SLTT	State, Local, Tribal and Territorial governments
USDA	Department of Agriculture
VA	Department of Veterans Affairs
WHO	World Health Organization

ENDNOTES

[1] Bipartisan Commission on Biodefense. (2015). A National Blueprint for Biodefense: Leadership and Major Reform Needed to Optimize Efforts. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/a-national-blueprint-for-biodefense/.

[2] Department of State. (2021). Adherence to and Compliance with Arms Control, Nonproliferation, and Disarmament Agreements and Commitments, pp. 46-52. Washington, DC: Department of State. Retrieved from: https://www.state.gov/wp-content/uploads/2021/04/2021-Adherence-to-and-Compliance-With-Arms-Control-Nonproliferation-and-Disarmament-Agreements-and-Commitments.pdf.

[3] Cutler, D. M., & Summers, L. H. (2020). The COVID-19 Pandemic and the $16 Trillion Virus. *JAMA*, 324(15), 1495–1496. https://doi.org/10.1001/jama.2020.19759.

[4] World Health Organization. (2020). WHO Coronavirus Disease (COVID-19) Dashboard. World Health Organization. Retrieved from: https://covid19.who.int.

[5] Blumenthal, D., Fowler, E. J., Abrams, M., & Collins, S. R. (2020). Covid-19—Implications for the Health Care System. *New England Journal of Medicine*, 383(15), 1483–1488. https://doi.org/10.1056/NEJMsb2021088.

[6] O'Donnell, L. B., Kristen E. Broady, Wendy Edelberg, and Jimmy. (2020, September 17). Ten Facts about COVID-19 and the US Economy. *Brookings*. Retrieved from: https://www.brookings.edu/research/ten-facts-about-covid-19-and-the-u-s-economy/.

[7] Allam, H. (2020). "Us Vs. Them" In A Pandemic: Researchers Warn Divisions Could Get Dangerous. *NPR*. Retrieved from: https://www.npr.org/sections/coronavirus-live-updates/2020/05/15/857165715/us-vs-them-in-a-pandemic-researchers-warn-divisions-could-get-dangerous.

[8] Center for Preventative Action. (2020). Peace, Conflict, and COVID-19. *Council on Foreign Relations*. Retrieved from: https://www.cfr.org/article/peace-conflict-and-covid-19.

[9] Marani, M., Katul, G. G., Pan, W. K., & Parolari, A. J. (2021). Intensity and frequency of extreme novel epidemics. *Proceedings of the National Academy of Sciences, 118*(35), e2105482118. https://doi.org/10.1073/pnas.2105482118.

[10] 10Rimmer, M. (2018). How smallpox claimed its final victim. *BBC News*. Retrieved from: https://www.bbc.com/news/uk-england-birmingham-45101091.

[11] Novossiolova, T., Minehata, M., & Dando, M. (2012). The Creation of a Contagious H5N1 Influenza Virus: Implications for the Education of Life Scientists. *Journal of terrorism research, 3*(1), 39–51. https://doi.org/10.15664/jtr.417.

[12] Miller, J. (2004). Russian Scientist Dies in Ebola Accident at Former Weapons Lab. *The New York Times.* Retrieved from: https://www.nytimes.com/2004/05/25/world/russian-scientist-dies-in-ebola-accident-at-former-weapons-lab.html.

[13] Lina, S.M.M., Kunasekaran, M.P. and Moa, A. (2021). Brucellosis Outbreak in China, 2019. *Global Biosecurity,* 3(1). Retrieved from: https://jglobalbiosecurity.com/articles/10.31646/gbio.108/.

[14] Bertrand, N., & Lippman, D. (2020, March 19). "It is not science fiction anymore": Coronavirus exposes US vulnerability to biowarfare. *POLITICO*. Retrieved from: https://www.politico.com/news/2020/03/19/coronavirus-biowarfare-terror-136194.

[15] COVID Data Tracker. (2022). United States COVID-19 Cases, Deaths, and Laboratory Testing (NAATs) by State, Territory, and Jurisdiction. Centers for Disease Control and Prevention. Retrieved from: https://covid.cdc.gov/covid-data-tracker/#cases_casesper100klast7days.

[16] Smith, K. F., Goldberg, M., Rosenthal, S., Carlson, L., Chen, J., Chen, C., & Ramachandran, S. (2014). Global rise in human infectious disease outbreaks. *Journal of the Royal Society Interface*, 11(101). https://doi.org/10.1098/rsif.2014.0950.

[17] Madhav, N., Oppenheim, B., Gallivan, M., Mulembakani, P., Rubin, E., & Wolfe, N. (2017). Pandemics: Risks, Impacts, and Mitigation. In Disease Control Priorities, Third Edition (Volume 9): Improving Health and Reducing Poverty (pp. 315–345). *The World Bank.* https://doi.org/10.1596/978-1-4648-0527-1_ch17.

[18] Gebreyes, W. A., Dupouy-Camet, J., Newport, M. J., Oliveira, C. J. B., Schlesinger, L. S., Saif, Y. M., Kariuki, S., Saif, L. J., Saville, W., Wittum, T., Hoet, A., Quessy, S., Kazwala, R., Tekola, B., Shryock, T., Bisesi, M., Patchanee, P., Boonmar, S., & King, L. J. (2014). The Global One Health Paradigm: Challenges and Opportunities for Tackling Infectious Diseases at the Human, Animal, and Environment Interface in Low-Resource Settings. *PLoS Neglected Tropical Diseases, 8(11)*, e3257. https://doi.org/10.1371/journal.pntd.0003257.

[19] Lina, S.M.M., Kunasekaran, M.P. and Moa, A. (2021). Brucellosis Outbreak in China, 2019. *Global Biosecurity,* 3(1). Retrieved from: https://jglobalbiosecurity.com/articles/10.31646/gbio.108/.

[20] Ellis, S., Wan, C., & Matsuyama, K. (2021). Mouse With Covid Sparks Taiwan Lab Alert After Biting Scientist. *Bloomberg.* Retrieved from: https://www.bloomberg.com/news/articles/2021-12-10/mouse-with-covid-sparks-lab-leak-alert-after-biting-scientist.

[21] Goad, M. (2021). A New Interactive Map Reveals Where the Deadliest Germs Are Studied. Schar School of Policy and Government, George Mason University. Retrieved from: https://schar.gmu.edu/news/2021-07/new-interactive-map-reveals-where-deadliest-germs-are-studied.

[22] National Academies of Sciences, Engineering, and Medicine. (2018). Biodefense in the Age of Synthetic Biology. Washington, DC: *The National Academies Press*. https://doi.org/10.17226/24890.

[23] Department of State. (2021). Adherence to and Compliance with Arms Control, Nonproliferation, and Disarmament Agreements and Commitments, pp. 46-52. Washington, DC: Department of State. Retrieved from: https://www.state.gov/wp-content/uploads/2021/04/2021-Adherence-to-and-Compliance-With-Arms-Control-Nonproliferation-and-Disarmament-Agreements-and-Commitments.pdf.

[24] "The effects of the current pandemic will obviously continue to strain governments and societies over the coming year, fueling humanitarian and economic crises, political unrest, and geopolitical competition as countries, such as China and Russia, seek advantage through "vaccine diplomacy" to build influence and in some cases demand accessions from other governments. Countries with high debts or that depend on oil exports, tourism, or remittances face particularly challenging recoveries, while others will turn inward or be distracted by other challenges. The critical impact of the pandemic has also served to highlight the importance of public health to national security." Haines, A. (2021). Remarks as prepared for delivery by The Honorable Avril Haines Director of National Intelligence. Annual Threat Assessment. Opening Statement. Senate Select Committee on Intelligence. Office of the Director of National Intelligence. Retrieved from: https://www.dni.gov/index.php/newsroom/congressional-testimonies/congressional-testimonies-2021/item/2206-dni-haines-opening-statement-on-the-2021-annual-threat-assessment-of-the-u-s-intelligence-community.

[25] National Intelligence Council. (2021). Global Trends 2040: A More Contested World. Office of the Director of National Intelligence. Retrieved from: https://www.dni.gov/index.php/gt2040-home.

[26] Musunuri, S., Sandbrink, J. B., Monrad, J. T., Palmer, M. J., & Koblentz, G. D. (2021). Rapid Proliferation of Pandemic Research: Implications for Dual-Use Risks. *MBio.* Published. https://doi.org/10.1128/mbio.01864-21. 28/mbio.01864-21.

[27] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats, p. 8. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[28] The White House. (2021). FACT SHEET: Biden Administration to Transform Capabilities for Pandemic Preparedness. The White House: Washington, DC. Retrieved from: https://www.whitehouse.gov/briefing-room/statements-releases/2021/09/03/fact-sheet-biden-administration-to-transform-capabilities-for-pandemic-preparedness/.

[29] Bipartisan Commission on Biodefense. (2021). Biodefense in Crisis: Immediate Action Needed to Address National Vulnerabilities. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/biodefense-in-crisis-immediate-action-needed-to-address-national-vulnerabilities/.

[30] For instance, in November 2021, the Secretary of Defense issued a biodefense vision memorandum for senior Pentagon leadership, combatant commanders, and defense agency and DOD field activity directors to direct the department to undertake a comprehensive Biodefense Posture Review. The memorandum identified three guiding principles for the posture review: (1) unify efforts through an empowered, collaborative, and integrated approach to biodefense across the department; (2) modernize DOD operations to optimize capabilities, capacity, resilience, and readiness; and (3) synchronize biodefense planning with the National Defense Strategy, efforts of other Federal departments and agencies, and allies and partners to support national biodefense efforts in alignment with national goals and strategy. Secretary of Defense. (2021). Memorandum for Senior Pentagon Leadership, Commanders of the Combatant Commands, Defense Agency, and DOD Field Activity Directors, Subject: Biodefense Vision. Washington, DC: Department of Defense. Retrieved from: https://media.defense.gov/2021/Dec/03/2002903201/-1/-1/0/BIODEFENSE-VISION-FINAL.PDF.

[31] Bipartisan Commission on Biodefense. (2015). A National Blueprint for Biodefense: Leadership and Major Reform Needed to Optimize Efforts, pp. 53-4. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/a-national-blueprint-for-biodefense/.

[32] Bipartisan Commission on Biodefense. (2015). A National Blueprint for Biodefense: Leadership and Major Reform Needed to Optimize Efforts, p. 56. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/a-national-blueprint-for-biodefense/.

[33] 33Bipartisan Commission on Biodefense. (2015). A National Blueprint for Biodefense: Leadership and Major Reform Needed to Optimize Efforts, p. 57. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/a-national-blueprint-for-biodefense/.

[34] Bipartisan Commission on Biodefense. (2015). A National Blueprint for Biodefense: Leadership and Major Reform Needed to Optimize Efforts, p. 58. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/a-national-blueprint-for-biodefense/.

[35] Bipartisan Commission on Biodefense. (2015). A National Blueprint for Biodefense: Leadership and Major Reform Needed to Optimize Efforts, p. 60. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/a-national-blueprint-for-biodefense/.

[36] Bipartisan Commission on Biodefense. (2015). A National Blueprint for Biodefense: Leadership and Major Reform Needed to Optimize Efforts, p. 61-2. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/a-national-blueprint-for-biodefense/.

[37] Bipartisan Commission on Biodefense. (2015). A National Blueprint for Biodefense: Leadership and Major Reform Needed to Optimize Efforts, p. 63. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/a-national-blueprint-for-biodefense/.

[38] In 2021, the Biden Administration released its American Pandemic Preparedness Plan which contains many recommendations from the Commission's Apollo Program for Biodefense. We consider this to be an example of an equivalent to The Apollo Program for Biodefense. The White House. (2021). FACT SHEET: Biden Administration to Transform Capabilities for Pandemic Preparedness. The White House: Washington, DC. Retrieved from: https://www.whitehouse.gov/briefing-room/statements-releases/2021/09/03/fact-sheet-biden-administration-to-transform-capabilities-for-pandemic-preparedness/.

[39] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[40] In 2021, the Biden Administration released its American Pandemic Preparedness Plan which contains many recommendations from the Commission's Apollo Program for Biodefense. We consider this to be an example of an equivalent to The Apollo Program for Biodefense. The White House. (2021). FACT SHEET: Biden Administration to Transform Capabilities for Pandemic Preparedness. The White House: Washington, DC. Retrieved from: https://www.whitehouse.gov/briefing-room/statements-releases/2021/09/03/fact-sheet-biden-administration-to-transform-capabilities-for-pandemic-preparedness/.

[41] In 2021, the Biden Administration released its American Pandemic Preparedness Plan which contains many recommendations from the Commission's Apollo Program for Biodefense. We consider this to be an example of an equivalent to The Apollo Program for Biodefense. The White House. (2021). FACT SHEET: Biden Administration to Transform Capabilities for Pandemic Preparedness. The White House: Washington, DC. Retrieved from: https://www.whitehouse.gov/briefing-room/statements-releases/2021/09/03/fact-sheet-biden-administration-to-transform-capabilities-for-pandemic-preparedness/.

[42] Congress required a unified, annual biodefense budget submission in Section 363 of the William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021 (P.L. 116-283, 6 USC 105).

[43] In 2021, the Biden Administration released its American Pandemic Preparedness Plan which contains many recommendations from the Commission's Apollo Program for Biodefense. We consider this to be an example of an equivalent to The Apollo Program for Biodefense. The White House. (2021). FACT SHEET: Biden Administration to Transform Capabilities for Pandemic Preparedness. The White House: Washington, DC. Retrieved from: https://www.whitehouse.gov/briefing-room/statements-releases/2021/09/03/fact-sheet-biden-administration-to-transform-capabilities-for-pandemic-preparedness/.

[44] In 2021, the Biden Administration released its American Pandemic Preparedness Plan which contains many recommendations from the Commission's Apollo Program for Biodefense. We consider this to be an example of an equivalent to The Apollo Program for Biodefense. The White House. (2021). FACT SHEET: Biden Administration to Transform Capabilities for Pandemic Preparedness. The White House: Washington, DC. Retrieved from: https://www.whitehouse.gov/briefing-room/statements-releases/2021/09/03/fact-sheet-biden-administration-to-transform-capabilities-for-pandemic-preparedness/.

[45] US Food and Drug Administration. (2021). FDA COVID-19 Pandemic Recovery and Preparedness (PREPP) Initiative: Summary Report. US Department of Health and Human Services. Retrieved from: https://www.fda.gov/media/145129/download.

[46] Krammer, F. (2020). Pandemic Vaccines: How Are We Going to Be Better Prepared Next Time? *Med, 1(1)*, 28–32. https://doi.org/10.1016/j.medj.2020.11.004.

[47] Graham, B. S., & Sullivan, N. J. (2018). Emerging viral diseases from a vaccinology perspective: preparing for the next pandemic. *Nature immunology, 19(1)*, 20-28. https://doi.org/10.1038/s41590-017-0007-9.

[48] Graham, B. S., & Corbett, K. S. (2020). Prototype pathogen approach for pandemic preparedness: world on fire. *The Journal of Clinical Investigation, 130(7)*. https://doi.org/10.1172/JCI139601.

[49] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats, p. 12. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[50] The White House. (2021). FACT SHEET: The American Jobs Plan. The White House: Washington, DC. Retrieved from: https://www.whitehouse.gov/briefing-room/statements-releases/2021/03/31/fact-sheet-the-american-jobs-plan/.

[51] The White House. (2021). FACT SHEET: The American Jobs Plan. The White House: Washington, DC. Retrieved from: https://www.whitehouse.gov/briefing-room/statements-releases/2021/03/31/fact-sheet-the-american-jobs-plan/.

[52] The White House. (2021). American Pandemic Preparedness: Transforming Our Capabilities. The White House: Washington, DC. Retrieved from: https://www.whitehouse.gov/wp-content/uploads/2021/09/American-Pandemic-Preparedness-Transforming-Our-Capabilities-Final-For-Web.pdf.

[53] The Coalition for Epidemic Preparedness Innovations. (2022). Global community comes together in support of 100 Days Mission and pledges over $1.5 billion for CEPI's pandemic-busting plan. CEPI. Retrieved from: https://cepi.net/news_cepi/global-community-comes-together-in-support-of-100-days-mission-and-pledges-over-1-5-billion-for-cepis-pandemic-busting-plan/.

[54] Graham, B. (2021). *Rapid COVID-19 Vaccine Development Enabled by Prototype Pathogen Preparedness* [Video 00:00-30:00]. Human Vaccines Project. Retrieved from: https://www.youtube.com/watch?v=ikZFKkiL1iM.

[55] Vigant, F., Santos, N. C., & Lee, B. (2015). Broad-spectrum antivirals against viral fusion. *Nature Reviews Microbiology, 13(7)*, 426-437. https://doi.org/10.1038/nrmicro3475.

[56] Adalja, A., & Inglesby, T. (2019). Broad-Spectrum Antiviral Agents: A Crucial Pandemic Tool. *Expert Rev Anti Infect Ther. 17(7)*: 467–470. https://dx.doi.org/10.1080%2F14787210.2019.1635009.

[57] Pannu, J. (2020). Running ahead of Pandemics: Achieving In-Advance Antiviral Drugs. Mercatus Center. http://dx.doi.org/10.2139/ssrn.3570737.

[58] 58Bekerman, E., & Einav, S. (2015). Combating emerging viral threats. Science, 348(6232), 282-283. https://doi.org/10.1126/science.aaa3778.

[59] Kelley, B. (2020). Developing therapeutic monoclonal antibodies at pandemic pace. *Nature biotechnology, 38*(5), 540-545. https://doi.org/10.1038/s41587-020-0512-5.

[60] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats, p. 13. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[61] Pannu, J. (2020). Broad-spectrum antiviral drugs: a survey of neglect. Future of Humanity Institute. University of Oxford. https://doi.org/10.31235/osf.io/kvjaz.

[62] Bekerman, E., & Einav, S. (2015). Combating emerging viral threats. *Science, 348*(6232), 282-283. https://doi.org/10.1126/science.aaa3778.

[63] Defense Advanced Research Projects Agency. (2021). Pandemic Prevention Platform (P3). US Department of Defense. Retrieved from: https://www.darpa.mil/program/pandemic-prevention-platform.

[64] Defense Advanced Research Projects Agency. (2021). Budget Justification Book FY2022. US Department of Defense. Retrieved from: https://www.darpa.mil/attachments/DARPA_PB_2022_19MAY2021_FINAL.pdf.

[65] Pannu, J. (2020). Broad-spectrum antiviral drugs: a survey of neglect. Future of Humanity Institute. University of Oxford. https://doi.org/10.31235/osf.io/kvjaz.

[66] Pannu, J. (2020). Running ahead of Pandemics: Achieving In-Advance Antiviral Drugs. Mercatus Center. http://dx.doi.org/10.2139/ssrn.3570737.

[67] Shiraki, K. & Daikoku, T. (2020). Favipiravir, an anti-influenza drug against life-threatening RNA virus infections. *Pharmacology & Therapeutics, 209.* https://doi.org/10.1016/j.pharmthera.2020.107512.

[68] US National Library of Medicine. (2021). Efficacy of Favipiravir in Treatment of Mild & Moderate COVID-19 Infection in Nepal. National Institutes of Health. Retrieved from: https://clinicaltrials.gov/ct2/show/NCT04694612.

[69] Pawlotsky, J. M. (2020). COVID-19 Pandemic: Time to Revive the Cyclophilin Inhibitor Alisporivir. *Clinical Infectious Diseases, 71*(16), 2191-2194. https://doi.org/10.1093/cid/ciaa587.

[70] Grogan, K. (2015). Novartis bids final farewell to HCV with Debiopharm exit. *PharmaTimes*. Retrieved from: http://www.pharmatimes.com/news/novartis_bids_final_farewell_to_hcv_with_debiopharm_exit_970847.

[71] Jackson, N. A., Kester, K. E., Casimiro, D., Gurunathan, S., & DeRosa, F. (2020). The promise of mRNA vaccines: A biotech and industrial perspective. *npj Vaccines, 5*(1), 1-6. https://doi.org/10.1038/s41541-020-0159-8.

[72] Kapoor, Y., Meyer, R. F., Meyer, B. K., DiNunzio, J. C., Bhambhani, A., Stanbro, J., ... & Templeton, A. C. (2021). Flexible Manufacturing: The Future State of Drug Product Development and Commercialization in the Pharmaceutical Industry. *Journal of Pharmaceutical Innovation, 1-9*. https://doi.org/10.1007/s12247-019-09426-z.

[73] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats, p. 14. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[74] Biomedical Advanced Research and Development Authority. (2012). Centers for Innovation in Advanced Development and Manufacturing. US Department of Health and Human Services. Retrieved from: https://www.medicalcountermeasures.gov/media/8862/aspa_0420_20120615_aspr_pr_countermeasures_fact_sheet_combined508.pdf.

[75] The Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense. (2021). Medical Countermeasures Advanced Development and Manufacturing. US Department of Defense. Retrieved from: https://www.jpeocbrnd.osd.mil/Portals/90/fact-sheet_adm.pdf.

[76] Hamby, C. (2021). Federal Government Cuts Ties with Troubled Vaccine Maker. *New York Times*. Retrieved from: https://www.nytimes.com/2021/11/04/us/emergent-biosolutions-covid-vaccine.html.

[77] Stanton, D. (2021). Emergent taking $180m hit as US Gov scraps CDMO contract. *BioProcess International.* Retrieved from: https://bioprocessintl.com/bioprocess-insider/deal-making/emergent-taking-180m-hit-as-us-gov-scraps-cdmo-contract/.

[78] Hamby, C. and Stolberg, S.G. (2021). Beneath a Covid Vaccine Debacle, 30 Years of Government Culpability. *The New York Times*. Retrieved from: https://www.nytimes.com/2021/12/23/us/covid-vaccine-biden-trump.html.

[79] Bipartisan Commission on Biodefense. (2021). Biodefense in Crisis: Immediate Action Needed to Address National Vulnerabilities. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/wp-content/uploads/2021/ 03/Indicators-Report_final7_070221_web.pdf.

[80] U.S. Food and Drug Administration. (2021). Advanced Manufacturing. U.S. Food and Drug Administration. Retrieved from: https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/advanced-manufacturing#fdarole.

[81] University of Oxford News and Events. (2021). Treating Needle Fears May Reduce COVID-19 Vaccine Hesitancy Rates by 10%. University of Oxford. Retrieved from: https://www.ox.ac.uk/news/2021-06-16-treating-needle-fears-may-reduce-covid-19-vaccine-hesitancy-rates-10.

[82] Prausnitz, M. R. (2017). Engineering microneedle patches for vaccination and drug delivery to skin. *Annual review of chemical and biomolecular engineering, 8*, 177-200. https://doi.org/10.1146/annurev-chembioeng-060816-101514.

[83] Ramirez, J. E. V., Sharpe, L. A., & Peppas, N. A. (2017). Current state and challenges in developing oral vaccines. *Advanced drug delivery reviews, 114,* 116-131. https://doi.org/10.1016/j.addr.2017.04.008.

[84] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats, p. 15. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[85] Pfizer Press Release. (2022). Pfizer to Provide U.S. Government with an Additional 10 Million Treatment Courses of its Oral Therapy to Help Combat COVID-19. Pfizer. Retrieved from: https://www.pfizer.com/news/press-release/press-release-detail/pfizer-provide-us-government-additional-10-million.

[86] Liebowitz, D., Gottlieb, K., Kolhatkar, N. S., Garg, S. J., Asher, J. M., Nazareno, J., Kim, K., McIlwain, D. R., & Tucker, S. N. (2020). Efficacy, immunogenicity, and safety of an oral influenza vaccine: a placebo-controlled and active-controlled phase 2 human challenge study. *The Lancet Infectious Diseases, 20*(4), 435-444. https://doi.org/10.1016/s1473-3099(19)30584-5.

[87] Assistant Secretary for Preparedness and Response Newsroom. (2021). HHS funds development of needle-free vaccine administration technology. US Department of Health and Human Services: Washington, DC. Retrieved from: https://aspr.hhs.gov/newsroom/Pages/ NewsDetailView.aspx?ItemID=458.

[88] National Science Foundation. (2021). Scientists developing inhalable COVID-19 vaccine spray. National Science Foundation. Retrieved from: https://nsf.gov/discoveries/disc_summ.jsp?cntn_id=303136&org=NSF&from=news.

[89] NIH Research Matters. (2021). Intranasal COVID-19 vaccine effective in animal studies. US Department of Health and Human Services. Retrieved from: https://www.nih.gov/news-events/nih-research-matters/intranasal-covid-19-vaccine-effective-animal-studies.

[90] BARDA Division of Research, Innovation, and Ventures. (2021). Beyond The Needle. Assistant Secretary for Preparedness and Response. Retrieved from: https://drive.hhs.gov/beyondtheneedle.html.

[91] Greninger, A. L., Naccache, S. N., Federman, S., Yu, G., Mbala, P., Bres, V., ... & Dodd, R. (2015). Rapid metagenomic identification of viral pathogens in clinical samples by real-time nanopore sequencing analysis. *Genome medicine, 7*(1), 99. https://doi.org/10.1186/s13073-015-0220-9.

[92] Erlich, Y. (2015). A vision for ubiquitous sequencing. *Genome research, 25*(10), 1411-1416. https://doi.org/10.1101/gr.191692.115.

[93] Samarakoon, H., Punchihewa, S., Senanayake, A., Hammond, J. M., Stevanovski, I., Ferguson, J. M., ... & Deveson, I. W. (2020). Genopo: a nanopore sequencing analysis toolkit for portable Android devices. *Communications biology, 3*(1), 1-5. https://doi.org/10.1038/s42003-020-01270-z.

[94] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats, p. 16. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[95] Maxmen, A. (2021). Why US coronavirus tracking can't keep up with concerning variants. *Nature, 592*(7854), 336–337. https://doi.org/10.1038/d41586-021-00908-0.

[96] Kirby, A. E., Walters, M. S., Jennings, W. C., Fugitt, R., LaCross, N., Mattioli, M., Marsh, Z. A., Roberts, V. A., Mercante, J. W., Yoder, J., & Hill, V. R. (2021). Using Wastewater Surveillance Data to Support the COVID-19 Response — United States, 2020–2021. *MMWR. Morbidity and Mortality Weekly Report, 70*(36), 1242–1244. https://doi.org/10.15585/mmwr.mm7036a2.

[97] The White House. (2021). FACT SHEET: Biden Administration Announces $1.7 Billion Investment to Fight COVID-19 Variants. The White House: Washington, DC. Retrieved from: https://www.whitehouse.gov/briefing-room/statements-releases/2021/04/16/fact-sheet-biden-administration-announces-1-7-billion-investment-to-fight-covid-19-variants/.

[98] Quer, G., Radin, J. M., Gadaleta, M., Baca-Motes, K., Ariniello, L., Ramos, E., ... & Steinhubl, S. R. (2020). Wearable sensor data and self-reported symptoms for COVID-19 detection. *Nature Medicine, 1-5.* https://doi.org/10.1038/s41591-020-1123-x.

[99] Filipiak, W., Ager, C., & Troppmair, J. (2017). Predicting the future from the past: volatile markers for respiratory infections. *European Respiratory Journal, 49*(5), 1700264. https://doi.org/10.1183/13993003.00264-2017.

[100] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats, p. 17. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[101] Tavares, F. (2021). NASA's E-Nose Device Advanced to "Sniff" COVID-19 from Human Breath. National Aeronautics and Space Administration Ames Research Center. Retrieved from: https://www.nasa.gov/feature/ames/e-nose.

[102] Ōura Blog. (2020). How Oura Ring Data Could Help Identify COVID-19 Symptoms. Ōura Health. Retrieved from: https://ouraring.com/blog/early-covid-symptoms/.

[103] Mason, A. E., Hecht, F. M., Davis, S. K., Natale, J. L., Hartogensis, W., Damaso, N., Claypool, K. T., Dilchert, S., Dasgupta, S., Purawat, S., Viswanath, V. K., Klein, A., Chowdhary, A., Fisher, S. M., Anglo, C., Puldon, K. Y., Veasna, D., Prather, J. G., Pandya, L. S., . . . Smarr, B. L. (2022). Detection of COVID-19 using multimodal data from a wearable device: results from the first TemPredict Study. *Scientific Reports, 12*(1). https://doi.org/10.1038/s41598-022-07314-0.

[104] Ates, H. C., Yetisen, A. K., Güder, F., & Dincer, C. (2021). Wearable devices for the detection of COVID-19. *Nature Electronics, 4*(1), 13–14. https://doi.org/10.1038/s41928-020-00533-1.

[105] Alavi, A., Bogu, G. K., Wang, M., Rangan, E. S., Brooks, A. W., Wang, Q., Higgs, E., Celli, A., Mishra, T., Metwally, A. A., Cha, K., Knowles, P., Alavi, A. A., Bhasin, R., Panchamukhi, S., Celis, D., Aditya, T., Honkala, A., Rolnik, B., . . . Snyder, M. P. (2021). Real-time alerting system for COVID-19 and other stress events using wearable data. *Nature Medicine, 28*(1), 175–184. https://doi.org/10.1038/s41591-021-01593-2.

[106] Munzert, S., Selb, P., Gohdes, A., Stoetzer, L. F., & Lowe, W. (2021). Tracking and promoting the usage of a COVID-19 contact tracing app. *Nature Human Behaviour, 5*(2), 247–255. https://doi.org/10.1038/s41562-020-01044-x.

[107] Hassibi, A., Manickam, A., Singh, R., Bolouki, S., Sinha, R., Jirage, K. B., ... & Pei, L. (2018). Multiplexed identification, quantification and genotyping of infectious agents using a semiconductor biochip. *Nature biotechnology, 36*(8), 738-745. https://doi.org/10.1038/nbt.4179.

[108] Palacios, G., Quan, P. L., Jabado, O. J., Conlan, S., Hirschberg, D. L., Liu, Y., ... & Grolla, A. (2007). Panmicrobial oligonucleotide array for diagnosis of infectious diseases. *Emerging infectious diseases, 13*(1), 73. https://dx.doi.org/10.3201%2Feid1301.060837.

[109] Wang, D., Urisman, A., Liu, Y. T., Springer, M., Ksiazek, T. G., Erdman, D. D., ... & Latreille, J. P. (2003). Viral discovery and sequence recovery using DNA microarrays. *PLoS Biology, 1*(2), e2. https://doi.org/10.1371/journal.pbio.0000002.

[110] Ackerman, C. M., Myhrvold, C., Thakku, S. G., Freije, C. A., Metsky, H. C., Yang, D. K., Ye, S. H., Boehm, C. K., Kosoko-Thoroddsen, T. S. F., Kehe, J., Nguyen, T. G., Carter, A., Kulesa, A., Barnes, J. R., Dugan, V. G., Hung, D. T., Blainey, P. C., & Sabeti, P. C. (2020). Massively multiplexed nucleic acid detection with Cas13. *Nature, 582*(7811), 277–282. https://doi.org/10.1038/s41586-020-2279-8.

[111] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats, p. 18. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[112] 360Dx. (2021). DARPA Awards $36.7M to Six Organizations for Gene Editing-Based Dx, Biosurveillance Tech. *GenomeWeb*. Retrieved from: https://www.360dx.com/research-funding/darpa-awards-367m-six-organizations-gene-editing-based-dx-biosurveillance-tech?_ga=2.30252988.2070085702.1634830563-1539840011.1634830562&adobe_ mc= MCMID%3D68289699599012498881133033381838762703%7CMCORGID%3D138FFF2554E6E7220A4C98C6%2540AdobeOrg%7CTS%3D1634830645&CSAuthResp=1%3A%3A2407862%3A1911%3A24%3Asuccess%3AC6B303922F67D95F85AB93118B7B4C95#.YXGSUrjMIQ9.

[113] Ackerman, C. M., Myhrvold, C., Thakku, S. G., Freije, C. A., Metsky, H. C., Yang, D. K., Ye, S. H., Boehm, C. K., Kosoko-Thoroddsen, T. S. F., Kehe, J., Nguyen, T. G., Carter, A., Kulesa, A., Barnes, J. R., Dugan, V. G., Hung, D. T., Blainey, P. C., & Sabeti, P. C. (2020). Massively multiplexed nucleic acid detection with Cas13. *Nature, 582*(7811), 277–282. https://doi.org/10.1038/s41586-020-2279-8.

[114] Engleman, K. (2019). Sherlock Biosciences Awarded Contract from U.S. Defense Threat Reduction Agency to Support the Development of Ultra-Fast, Ultra-Sensitive Diagnostics. *BusinessWire.* Retrieved from: https://www.businesswire.com/news/home/20190926005044/en/Sherlock-Biosciences-Awarded-Contract-from-U.S.-Defense-Threat-Reduction-Agency-to-Support-the-Development-of-Ultra-Fast-Ultra-Sensitive-Diagnostics.

[115] Rapid Acceleration of Diagnostics (RADx). (2021). Governance of RADx Programs. National Institutes of Health: Washington, DC. Retrieved from: https://www.nih.gov/research-training/medical-research-initiatives/radx/governance.

[116] Bipartisan Commission on Biodefense. (2021). Saving Sisyphus: Advanced Biodetection for the 21st Century. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/saving-sisyphus-advanced-biodetection-for-the-21st-century/.

[117] Bipartisan Commission on Biodefense. (2015). A National Blueprint for Biodefense: Leadership and Major Reform Needed to Optimize Efforts, 58. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/a-national-blueprint-for-biodefense/.

[118] Bipartisan Commission on Biodefense (2020). Diagnostics for Biodefense: Flying Blind with No Plan to Land. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/diagnostics-for-biodefense-flying-blind-with-no-plan-to-land/.

[119] Mina, M. J., Parker, R., & Larremore, D. B. (2020). Rethinking Covid-19 test sensitivity—A strategy for containment. *New England Journal of Medicine, 383*(22), e120. https://www.nejm.org/doi/full/10.1056/nejmp2025631.

[120] Centers for Disease Control and Prevention (2021). Guidance for SARS-CoV-2 Point-of-Care Testing. US Department of Health and Human Services. Retrieved from: https://www.cdc.gov/coronavirus/2019-ncov/lab/point-of-care-testing.html.

[121] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats, p. 19. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[122] Rapid Acceleration of Diagnostics (RADx). (2021). Governance of RADx Programs. National Institutes of Health: Washington, DC. Retrieved from: https://www.nih.gov/research-training/medical-research-initiatives/radx/governance.

[123] Bogoch, I. I., Watts, A., Thomas-Bachli, A., Huber, C., Kraemer, M., & Khan, K. (2020). Pneumonia of unknown aetiology in Wuhan, China: potential for international spread via commercial air travel. *Journal of travel medicine, 27*(2), taaa008. https://doi.org/10.1093/jtm/taaa008.

[124] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats, p. 19. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[125] Metabiota. (2021). Scientific and Policy Publications. Metabiota. Retrieved from: https://metabiota.com/publications.

[126] Steig, C. (2020). How this start-up spotted coronavirus before everyone else knew about it. *CNBC News.* Retrieved from: https://www.cnbc.com/2020/03/03/bluedot-used-artificial-intelligence-to-predict-coronavirus-spread.html.

[127] Office of the National Coordinator for Health Information Technology. (2021). About ONC. US Department of Health and Human Services: Washington, DC. Retrieved from: https://www.healthit.gov/topic/about-onc.

[128] Aftergood, S. (2015). Open Source Center (OSC) Becomes Open Source Enterprise (OSE). Federation of American Scientists. Retrieved from: https://fas.org/blogs/secrecy/2015/10/osc-ose/.

[129] WHO Health Topics. (2021). Infodemic. World Health Organization. Retrieved from: https://www.who.int/health-topics/infodemic#tab=tab_1.

[130] Safran, C., Bloomrosen, M., Hammond, W. E., Labkoff, S., Markel-Fox, S., Tang, P. C., & Detmer, D.E. (2007). Toward a national framework for the secondary use of health data: an American Medical Informatics Association White Paper. *Journal of the American Medical Informatics Association, 14*(1), 1-9. https://dx.doi.org/10.1197%2Fjamia.M2273.

[131] National Academies of Sciences, Engineering, and Medicine. (2020). Genomic Epidemiology Data Infrastructure Needs for SARS-CoV-2: Modernizing Pandemic Response Strategies. Washington, DC: *National Academies Press.* https://doi.org/10.17226/25879.

[132] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats, p. 20. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[133] US Centers for Disease Control and Prevention. (2021). CDC's Data Modernization Initiative. US Department of Health and Human Services. Retrieved from: https://www.cdc.gov/surveillance/projects/dmi-initiative/index.html.

[134] George, D. B., Taylor, W., Shaman, J., Rivers, C., Paul, B., O'Toole, T., ... & Reich, N. G. (2019). Technology to advance infectious disease forecasting for outbreak management. Nature communications, 10(1), 1-4. https://doi.org/10.1038/s41467-019-11901-7.

[135] Rivers, C., Martin, E., Meyer, D., Inglesby, T. V., & Cicero, A. J. (2020). Modernizing and Expanding Outbreak Science to Support Better Decision Making During Public Health Crises: Lessons for COVID-19 and Beyond. Johns Hopkins Center for Health Security. Retrieved from: https://www.centerforhealthsecurity.org/our-work/publications/modernizing-and-expanding-outbreak-science-to-support-better-decision-making-during-public-health-crises.

[136] Press, W. H., & Levin, R. C. (2020). Modeling, post COVID-19. Science. https://doi.org/10.1126/science.abf7914.

[137] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats, p. 21. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[138] CDC Newsroom. (2021). CDC Stands Up New Disease Forecasting Center. US Centers for Disease Control and Prevention. Retrieved from: https://www.cdc.gov/media/releases/2021/p0818-disease-forecasting-center.html.

[139] Radonovich Jr, L. J., Roberge, R., Baig, A., Levinson, A., Shaffer, R. E., Doerr, D. F., & Davey, V. (2009). Better respirator equipment using advanced technologies for healthcare employees (Project BREATHE): An interagency working group of the US federal government. Office of Public Health and Environmental Hazards, Veterans Health Administration, US Department of Veterans Affairs. Retrieved from: https://www.cdc.gov/niosh/npptl/hospresptoolkit/pdfs/ProjectBREATHE-final-report-508.pdf.

[140] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats, p. 22. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[141] RePORTER. (2021). Validation of Smart Masks for Surveillance of COVID-19. US National Institutes of Health: Washington, DC. Retrieved from: https://reporter.nih.gov/project-details/10273452.

[142] Jet Propulsion Laboratory. (2020). PAPR | The COVID-19 Powered Air-Purifying Respirator. National Aeronautics and Space Administration. Retrieved from: https://medeng.jpl.nasa.gov/covid-19/papr/.

[143] NASA Glenn Research Center. (2020). NASA, University Hospitals Join Forces in Response to COVID-19. National Aeronautics and Space Administration. Retrieved from: https://www.nasa.gov/press-release/glenn/2020/nasa-university-hospitals-join-forces-in-response-to-covid-19.

[144] Lincoln Advanced Technologies. (2021). A new generation of masks for protection at the hospital, in the field, at work and at home. Lincoln Advanced Technologies. Retrieved from: https://lincolnadvanced.net.

[145] BARDA Division of Research, Innovation, and Ventures. (2021). Mask Innovation Challenge: Building Tomorrow's Mask. Assistant Secretary for Preparedness and Response. Retrieved from: https://drive.hhs.gov/mask_challenge.html.

[146] Wei, J., & Li, Y. (2016). Airborne spread of infectious agents in the indoor environment. *American journal of infection control, 44*(9), S102-S108. https://doi.org/10.1016/j.ajic.2016.06.003.

[147] Ding, J., Yu, C. W., & Cao, S. J. (2020). HVAC systems for environmental control to minimize the COVID-19 infection. *Indoor and Built Environment, 29*(9), 1195-1201. https://doi.org/10.1177%2F1420326X20951968.

[148] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats, p. 23. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[149] Berman, J. (2021). 'This is a significant amount of money': COVID-19 relief bill would send nearly $170 billion to schools. *MarketWatch*. Retrieved from: https://www.marketwatch.com/story/this-is-a-significant-amount-of-money-covid-19-relief-bill-would-send-nearly-170-billion-to-schools-11615223919.

[150] Nierenberg, A., Taylor, K. (2021). How Can Schools Use $129 Billion in Covid Relief Funds? *The New York Times.* Retrieved from: https://www.nytimes.com/2021/03/24/us/covid-schools-federal-funding.html.

[151] "The Public Buildings Amendments of 1988, 40 U.S.C. 3312 require that each building constructed or altered by GSA or any other federal agency shall, to the maximum extent feasible, be in compliance with one of the nationally recognized model building codes and with other applicable nationally recognized codes." General Services Administration. (2019). Codes and Standards. General Services Administration. Retrieved from: https://www.gsa.gov/cdnstatic/Chapter_1_General_Requirements.pdf.

[152] Thompson, T. (2021). Real-world data show that filters clean COVID-causing virus from air. *Nature.* Published. https://doi.org/10.1038/d41586-021-02669-2.

[153] Wade, N. (1978). New smallpox case seems lab-caused. *Science, 201*(4359), 893-893. https://doi.org/10.1126/science.684414.

[154] Meselson, M., Guillemin, J., Hugh-Jones, M., Langmuir, A., Popova, I., Shelokov, A., & Yampolskaya, O. (1994). The Sverdlovsk anthrax outbreak of 1979. *Science, 266*(5188), 1202-1208. https://doi.org/10.1126/science.7973702.

[155] Nakajima, K., Desselberger, U., & Palese, P. (1978). Recent human influenza A (H1N1) viruses are closely related genetically to strains isolated in 1950. *Nature, 274*(5669), 334-339. https://doi.org/10.1038/274334a0.

[156] Musunuri, S., Sandbrink, J. B., Monrad, J. T., Palmer, M. J., & Koblentz, G. D. (2021). Rapid Proliferation of Pandemic Research: Implications for Dual-Use Risks. *MBio.* https://doi.org/10.1128/mbio.01864-21.

[157] Kojima, K., Booth, C. M., Summermatter, K., Bennett, A., Heisz, M., Blacksell, S. D., & McKinney, M. (2018). Risk-based reboot for global lab biosafety. *Science, 360*(6386), 260–262. https://doi.org/10.1126/science.aar2231.

[158] Ritterson, R., & Casagrande, R. (2017). Basic Scholarship in Biosafety Is Critically Needed To Reduce Risk of Laboratory Accidents. *MSphere, 2*(2). https://doi.org/10.1128/msphere.00010-17.

[159] "...The best-designed and most engineered laboratory is only as good as its least competent worker." Kojima, K., Booth, C. M., Summermatter, K., Bennett, A., Heisz, M., Blacksell, S. D., & McKinney, M. (2018). Risk-based reboot for global lab biosafety. *Science, 360*(6386), 260–262. https://doi.org/10.1126/science.aar2231.

[160] Gillum, D., Vogel, K., Moritz, R. (2021) Reporting all biosafety errors could improve labs worldwide – and increase public trust in biological research. *The Conversation.* Retrieved from: https://theconversation.com/reporting-all-biosafety-errors-could-improve-labs-worldwide-and-increase-public-trust-in-biological-research-168552.

[161] Ritterson, R., & Casagrande, R. (2017). Basic Scholarship in Biosafety Is Critically Needed To Reduce Risk of Laboratory Accidents. *MSphere, 2*(2). https://doi.org/10.1128/msphere.00010-17.

[162] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats, p. 24. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[163] Office of the Assistant Secretary for Preparedness and Response. (2017). Biosafety FAQ's - Oversight. US Department of Health and Human Services: Washington, DC. Retrieved from: https://www.phe.gov/s3/BioriskManagement/biosafety/Pages/Biosafety-FAQ.aspx#over.

[164] Office of Science Policy. (2020). National Science Advisory Board for Biosecurity (NSABB). National Institutes of Health: Washington, DC. Retrieved from: https://osp.od.nih.gov/biotechnology/national-science-advisory-board-for-biosecurity-nsabb/#about.

[165] Ritterson, R., & Casagrande, R. (2017). Basic Scholarship in Biosafety Is Critically Needed To Reduce Risk of Laboratory Accidents. MSphere, 2(2). Retrieved from: https://doi.org/10.1128/msphere.00010-17.

[166] National Institute of Allergy and Infectious Diseases. (2018). The Need for Biosafety Labs. National Institutes of Health: Washington, DC. Retrieved from: https://www.niaid.nih.gov/research/biosafety-labs-needed.

[167] Lewis, G., Jordan, J. L., Relman, D. A., Koblentz, G. D., Leung, J., Dafoe, A., ... & Alley, E. C. (2020). The biosecurity benefits of genetic engineering attribution. *Nature Communications, 11*(1), 1-4. https://doi.org/10.1038/s41467-020-19149-2.

[168] Alley, E. C., Turpin, M., Liu, A. B., Kulp-McDowall, T., Swett, J., Edison, R., ... & Esvelt, K. M. (2020). A machine learning toolkit for genetic engineering attribution to facilitate biosecurity. *Nature Communications, 11*(1), 1-12. https://doi.org/10.1038/s41467-020-19612-0.

[169] National Academies of Sciences, Engineering, and Medicine. (2018). "Options for Mitigating Concerns." Biodefense in the Age of Synthetic Biology. Washington DC: *National Academies Press.* https://www.nap.edu/read/24890/chapter/10.

[170] Bipartisan Commission on Biodefense. (2021). The Apollo Program for Biodefense: Winning the Race Against Biological Threats, p. 24. Washington, DC: Bipartisan Commission on Biodefense. Retrieved from: https://biodefensecommission.org/reports/the-apollo-program-for-biodefense-winning-the-race-against-biological-threats/.

[171] Intelligence Advanced Research Projects Activity. (2021). Functional Genomic and Computational Assessment of Threats (Fun GCAT). Office of the Director of National Intelligence. Retrieved from: https://www.iarpa.gov/index.php/research-programs/fun-gcat.

[172] Intelligence Advanced Research Projects Activity. (2021). Finding Engineering-Linked Indicators (FELIX). Office of the Director of National Intelligence. Retrieved from: https://www.iarpa.gov/index.php/research-programs/felix.

[173] altLabs. (2021). Genetic Engineering Attribution Challenge. AltLabs. Retrieved from: https://altlabs.tech/geac/.

[174] MIT Media Lab. (2021). Secure DNA Project. Massachusetts Institute of Technology. Retrieved from: https://www.media.mit.edu/projects/secure-dna/overview/.

[175] Assistant Secretary for Preparedness and Response. (2010). Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA. US Department of Health and Human Services. Retrieved from: https://www.phe.gov/Preparedness/legal/guidance/syndna/Pages/default.aspx.

[176] California Legislature. (2021). AB-70 Gene synthesis providers. California Legislature. Retrieved from: https://leginfo.legislature.ca.gov/faces/billTextClient.xhtml?bill_id=202120220AB70.

[177] Maryland House of Delegates. (2021). HB1256. Maryland Department of Health – Gene Synthesis Providers and Manufacturers of Gene Synthesis Equipment – Certification. Maryland General Assembly. Retrieved from: https://mgaleg.maryland.gov/mgawebsite/Legislation/Details/hb1256?ys=2021RS.

[178] International Gene Synthesis Consortium. (2021). About IGSC. International Gene Synthesis Consortium. Retrieved from: https://genesynthesisconsortium.org/.

[179] Example of best practices. For more information see International Gene Synthesis Consortium. (2017). Harmonized Screening Protocol. International Gene Synthesis Consortium. Retrieved from: https://genesynthesisconsortium.org/wp-content/uploads/IGSCHarmonizedProtocol11-21-17.pdf.

[180] The State of Hawaii eventually managed to change FEMA's decisions in this regard when the Governor said that they would decline FEMA-purchased telephone poles and wire and requested that the funds be given to the State instead (so that it could purchase and bury fiber optic cables), insisting that the State would rather go without telephone service than perpetually reinstall old technology that would only get destroyed with every successive hurricane.

[181] Logsdon, J. M. (2018). *Ronald Reagan and the Space Frontier (Palgrave Studies in the History of Science and Technology)* (1st ed. 2019 ed.). Palgrave Macmillan.

[182] Wang, M. (2017). The Role of Panama Canal in Global Shipping. *Maritime Business Review,* 2(3), 247-260. https://doi.org/10.1108/mabr-07-2017-0014.

[183] The Economist. (2016). *Wider Impact.* Retrieved from: https://www.economist.com/business/2016/06/18/wider-impact.

[184] Brown, M. (2018). Welcome to the Neo-Panamax Era: Big Ships, Big Opportunities. *Inbound Logistics.* Retrieved from: https://www.inboundlogistics.com/cms/article/neo-panamax-era-arrives-why-shippers-should-take-notice/.

[185] Rai, A., Robinson, J. A., Tate-Brown, J., Buckley, N., Zell, M., Tasaki, K., Karabadzhak, G., Sorokin, I. V., & Pignataro, S. (2016). Expanded Benefits for Humanity from the International Space Station. *Acta Astronautica, 126,* 463-474. https://doi.org/10.1016/j.actaastro.2016.06.030.

[186] NewsThink. (2020). *The Future of the International Space Station* [Video]. YouTube. Retrieved from: https://www.youtube.com/watch?v=D82Ds4MeUKI&t=62s.

[187] Koman, R. G. (1994). Man on the Moon: The US Space Program as a Cold War Maneuver. *OAH Magazine of History*, 8(2), 42-50. http://www.jstor.org/stable/25162945.

[188] Watanabe, H. (2009). The Kennedy Administration and Project Apollo: International Competition and Cooperation through Space Policy. *Osaka University Law Review*, 56, 31-48. Retrieved from: https://ir.library.osaka-u.ac.jp/repo/ouka/all/9916/oulr056-031.pdf.

[189] Al Takarli, N. S. (2020). China's Response to the COVID-19 Outbreak: A Model for Epidemic Preparedness and Management. *Dubai Medical Journal,* 3(2), 44-49. https://doi.org/10.1159/000508448.

[190] Hjelmgaard, K., Lyman, E. J., & Shesgreen, D. (2020). This Is What China Did to Beat Coronavirus. Experts Say America Couldn't Handle It. *USA Today.* Retrieved from: https://www.usatoday.com/story/news/world/2020/04/01/coronavirus-covid-19-china-radical-measures-lockdowns-mass-quarantines/2938374001/.

[191] Blas, E. (2010). The Dwight D. Eisenhower National System of Interstate and Defense Highways: The Road to Success? *The History Teacher,* 44(1), 127-142. https://www.jstor.org/stable/25799401.

[192] Blas, E. (2010). The Dwight D. Eisenhower National System of Interstate and Defense Highways: The Road to Success? *The History Teacher,* 44(1), 127-142. https://www.jstor.org/stable/25799401.

[193] GPS World Staff. (2021). Part 1: The Origins of GPS, and the Pioneers Who Launched the System. *GPS World.* Retrieved from: https://www.gpsworld.com/origins-gps-part-1/.

[194] Guier, W. H., & Weiffenbach, G. C. (1998). Genesis of Satellite Navigation. *Johns Hopkins APL Technical Digest,* 19(1), 15. Retrieved from: https://www.jhuapl.edu/content/techdigest/pdf/v19-n01/19-01-guier.pdf.

[195] Rip, M. R., & Hasik, J. M. (2002). *The Precision Revolution: GPS and the Future of Aerial Warfare* (1st ed.). Annapolis, MD: Naval Institute Press.

[196] Parthemore, C.& Weber, A. (2021). The US must separate nuclear deterrence from biological weapons. *Defense News*. Retrieved from: https://www.defensenews.com/opinion/commentary/2021/10/18/the-us-must-separate-nuclear-deterrence-from-biological-weapons/.

[197] Bennett, I. E., & Hammond, J. H. (1915). *History of the Panama Canal: Its Construction and Builders.* Washington, DC: Historical Publishing Company.

[198] McCullough, D. (2001). *The Path Between the Seas: The Creation of the Panama Canal, 1870-1914.* New York, NY: Simon & Schuster.

[199] Avery, R. E. (1913). The French Failure. In *America's Triumph at Panama.* Chicago, IL: L.W. Walter Company.

[200] Lowrie, W. E. (1975). *France, the United States, and the Lesseps Panama Canal: Renewed Rivalry in the Western Hemisphere, 1879-1889.* Syracuse, NY: Syracuse University.

[201] TED Education. (2021). *Demolition, Disease, and Death: Building the Panama Canal – Alex Gendler* [Video]. YouTube. Retrieved from: https://www.youtube.com/watch?v=uE_UuHRtXCY.

[202] Fenner, F. (1982). Global Eradication of Smallpox. *Reviews of Infectious Diseases* 4(5), 916-930. https://doi.org/10.1093/clinids/4.5.916.

[203] Rimmer, B. M. (2018). How Smallpox Claimed Its Final Victim. *BBC News.* Retrieved from: https://www.bbc.com/news/uk-england-birmingham-45101091.

[204] Tripp, S., & Grueber M. (2011). Economic Impact of the Human Genome Project: How a $3.8 Billion Investment Drove $796 Billion in Economic Impact, Created 310,000 Jobs and Launched the Genomic Revolution. *Battelle Memorial Institute.* Retrieved from: https://www.battelle.org/docs/default-source/misc/battelle-2011-misc-economic-impact-human-genome-project.pdf.

[205] HHS Press Office. (2020). Trump Administration Announces Framework and Leadership for 'Operation Warp Speed. US Department of Health and Human Services. Retrieved from: https://www.hhs.gov/about/news/2020/05/15/trump-administration-announces-framework-and-leadership-for-operation-warp-speed.html.

[206] Patton, M. (2021). The Impact of Covid-19 on US Economy and Financial Markets. *Forbes Magazine.* Retrieved from: https://www.forbes.com/sites/mikepatton/2020/10/12/the-impact-of-covid-19-on-us-economy-and-financial-markets/?sh=4585249d2d20.

[207] Patton, M. (2021). The Impact of Covid-19 on US Economy and Financial Markets. *Forbes Magazine.* Retrieved from: https://www.forbes.com/sites/mikepatton/2020/10/12/the-impact-of-covid-19-on-us-economy-and-financial-markets/?sh=4585249d2d20.

[208] Blas, E. (2010). The Dwight D. Eisenhower National System of Interstate and Defense Highways: The Road to Success? *The History Teacher,* 44(1), 127-142. https://www.jstor.org/stable/25799401.

[209] The European Space Agency (2021). International Space Station Legal Framework. The European Space Agency. Retrieved from: https://www.esa.int/Science_Exploration/ Human_and_Robotic_Exploration/International_Space_Station/International_Space_Station_legal_framework.

[210] Wheeler, W. H. (1895). Ferdinand de Lesseps and the Suez and Panama Canals. *Longman's Magazine,* 1882-1905, 25(148), 394-411.

[211] Avery, R. E. (1913). The French Failure. In *America's Triumph at Panama.* Chicago, IL: L.W. Walter Company.

[212] McCullough, D. (2001). The Path Between the Seas: *The Creation of the Panama Canal, 1870-1914.* New York, NY: Simon & Schuster.

[213] Young, A. (2015). NASA Commercial Partnerships. In *The Twenty-First Century Commercial Space Imperative* (pp. 43-57). Springer.

BIPARTISAN COMMISSION ON BIODEFENSE

www.biodefensecommission.org