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VIA CM/ECF

June 13, 2023

Ms. Patricia S. Dodszuweit, Clerk
U.S. Court of Appeals for the
Third Circuit
21400 U.S. Courthouse
601 Market Street
Philadelphia, PA 19106

RE: Sczesny v. Murphy, No. 22-2230 (3d Cir.)

Dear Ms. Dodszuweit:

This letter is submitted in response to the State's June 12, 2023 letter advising the panel that Governor Murphy has rescinded the pharmaceutical mandate challenged in this action and for which an injunction was sought through this appeal. New Jersey declares that "the appeal is now moot." However, it is well-settled that a defendant "does not deprive a federal court of its power to determine the legality of [a] practice," simply by stopping the practice. So long as the complaining party maintains a personal stake in the outcome for which the Court could provide effectual and meaningful relief, the judicial branch of government retains jurisdiction to do its duty. *Campbell-Ewald Co. v. Gomez*, 577 *U.S.* 153, 160–61 (2016), as revised (Feb. 9, 2016) (noting that "[a] case becomes moot…only when it is impossible for a court to grant any effectual relief whatever to the prevailing

party" and "[a]s long as the parties have a concrete interest, however small, in the outcome of the litigation, the case is not moot") (internal citations omitted).

Here the appeal and the case are not moot because: 1) the controversy is still live and this Court can grant the Nurses meaningful and effective relief, 2) the voluntary cessation doctrine applies, and 3) the pharmaceutical mandate is capable of repetition and evading review.

ARGUMENT

I. There is still a live controversy with regard to EO 283 because rescinding it did not extinguish residual and continuing effects of the coercive mandate and the Court can provide meaningful relief

The controversy before this panel and the relief sought is the same and just as meaningful today as it was when the Nurses first availed themselves of the judicial system by filing a Complaint thirteen months ago. The controversy is whether the State of New Jersey and its Governor can coerce the Nurses to be injected with an emergency pharmaceutical on pain of losing their jobs or whether they have the liberty to refuse. The relief sought is a declaration that EO 283 is/was unconstitutional. *See* Exhibit A (prayer for relief from Complaint).

All the Nurses lost their jobs because of EO 283. Katie Sczesny, Mariette Vitti, and Jaime Rumfield were all terminated for cause for not complying with EO 283. This is a blemish on their employment records. This court can provide meaningful relief because, for the Nurses, it is the difference between having been

terminated for insubordination and having been terminated for standing up for their constitutional rights.

In addition to declaratory relief, the Nurses seek attorney fees pursuant to §1988, as to Governor Murphy who is sued in his personal capacity. *See* Exhibit 1. These damages prevent the case from becoming moot as against Governor Murphy and a declaration that EO 283 is unconstitutional will narrow the issue on remand to one of qualified immunity. Conversely, a declaration that it is constitutional under the 14th Amendment will dispose of much of the Complaint.

Finally, while EO 322 repeals the pharmaceutical mandate, it is very explicit that:

> Nothing in this Order shall prevent covered settings from choosing to maintain a COVID-19 vaccination or testing policy, including but not limited to, one implemented pursuant to Executive Order No. 252 (2021), Executive Order Nos. 283, 290, and 294 (2022), Paragraph 2 of Executive Order No. 281 (2022), and Executive Order No. 325 (2023), or from establishing a COVID-19 vaccination or testing policy that includes additional or stricter requirements.

Because every covered entity was required to adopt a pharmaceutical mandate policy pursuant to EO 283, the persistence of the mandates constitutes a continuing controversy on their own. The fact that the State is putting its imprimatur of approval on such mandates continues the case and controversy as well. Judicial recognition of the Nurses' liberty will remove the imprinter of state approval from mandates

erected pursuant to EO 283 and maintained pursuant to the encouragement of EO 322.

A. The case and the appeal are not moot because there is an ongoing constitutional controversy between the Nurses and the State and this court can provide meaningful relief

The Governor and the Nurses both claim the right to determine what medical procedures will be done to the Nurses' bodies and both claim their authority from the Constitution. The Nurses point to the Fourteenth Amendment substantive due process clause. The Governor points to the state police power. The question of where this power lies is an ongoing controversy over which this court has jurisdiction.

This is an adversarial, genuine, and ongoing controversy, the resolution of which will provide meaningful relief to the Nurses by settling their rights over their own bodies, which are quite meaningful, and provide judicial recognition that their termination from employment was pursuant to an unconstitutional order. Moreover, it will settle the question of what is the proper level of review.

II. Even if there were not an existing case or controversy, the doctrine of voluntary cessation applies

A Defendant's voluntary cessation of an allegedly unlawful behavior is presumptively NOT moot and "[t]he Government bears the burden to establish that a once-live case has become moot." *W. Virginia v. Env't Prot. Agency*, 213 L. Ed. 2d 896, 142 S. Ct. 2587, 2594 (2022). This is a "formidable burden of showing that it is absolutely clear the allegedly wrongful behavior could not reasonably be

expected to recur." *Friends of the Earth, Inc. v. Laidlaw Envtl. Servs. (TOC), Inc.*, 528 U.S. 167, 190 (2000); *see also Parents Involved in Community Schools v. Seattle School Dist. No. 1*, 551 U.S. 701, 719 (2007). It is an especially "heavy" burden in a case like this one where, "[t]he only conceivable basis for a finding of mootness in the case is [the Defendant's] voluntary conduct." *W. Virginia v. Env't Prot. Agency*, 213 L. Ed. 2d 896, 142 S. Ct. 2587, 2607 (2022)(cleaned up and internal citations omitted); *see also Friends of the Earth*, 528 U.S. at 189 (stating that "[i]t is well settled that "a defendant's voluntary cessation of a challenged practice does not deprive a federal court of its power to determine the legality of the practice").

The Supreme Court has stated that when a Defendant has voluntarily withdrawn a challenged policy that is the basis of litigation but continues to "vigorously defend" the legality of its action, the claim remains justiciable. *W. Virginia v. Env't Prot. Agency*, 142 S. Ct. 2587, 2607 (2022) (citing *City of Mesquite v. Aladdin's Castle, Inc.*, 455 U.S. 283, 288–289 (1982).

Here, the voluntary cessation doctrine precludes a finding of mootness. As an initial matter, it is difficult to see how the Court could find that it is "absolutely clear" that this situation will not arise again when the State itself makes no such representation. On the contrary, the State's purported reasoning/rationalizations as to why the mandate could be ended are credited largely to the mandate's purported success. Moreover, as the panel will recall, the State vigorously defended its policy

of coerced booster shots even in the absence of an emergency.

Finally, in its letter to the panel, the State highlights the withdrawal of the CMS mandate as a reason to withdraw EO 283. However, this obscures the fact that these Nurses were in compliance with the CMS mandate; they are all fully vaccinated. In addition, it obscures the true reason for EO 283's withdrawal: the exact shots that were mandated by EO 283 have had their authorization withdrawn. However, Governor Murphy can sign an executive order tomorrow mandating the bivalent booster and the State of New Jersey has vigorously defended his right to do so under any circumstances he deems appropriate. The same controversy remains, particularly concerning the proper level of review. Most importantly, the State knows that it must be absolutely clear that the mandate is not likely to recur for this Court to lose jurisdiction, but the State made no representation that it will not reenact the mandate if Governor Murphy's judgment about the importance of the bivalent booster changes.

III. Even if there were not an existing case or controversy, the controversy is capable of repetition and avoiding review and is therefore not moot

A. The Mandates are, demonstrably, capable of avoiding review

The State's letter makes clear: covid era mandates are uniquely capable of avoiding review. *See* State's June 12, 2023 letter, ECF 61 at pg. 2 (listing the "chorus" of covid-era decisions that have been dismissed as moot). These cases <u>are</u> evading review, so they are clearly capable of avoiding review.

B. The Mandates are capable of repetition

Governor Murphy, in every executive order put before this Court as part of this litigation, has pointed to the federal government as its source for guidance. Thus, the fact that the federal government has stated that "there is a reasonable likelihood that another serious pandemic that may be worse than COVID-19 will occur soon" and that the rapid development and deployment of vaccines (within 130 days of identifying the virus) is the planned response, indicate that repetition is likely. *See* Exhibit B, The White House, *American Pandemic Preparedness: Transforming Our Capabilities*, at pages 5 and 11 (stating that top goals of pandemic preparedness will be to have a vaccine ready to go 130 days after a potential threat has been identified). The fact that repetition is likely makes review by this court even more urgent because there is a controversy concerning the standard of review on which few Circuit Courts of Appeal have opined.

In addition, the procedures and infrastructure put in place by these mandates along with the simple fact that it happened once, increase the likelihood of it happening again and even faster. A path already trodden is easier to take again. The fact that the specific policies were withdrawn is irrelevant if the procedures remain in place to institute a substantially similar policy with the strike of a pen. It is, therefore, notable, that the State explicitly is keeping some policies and procedures in place and implicitly encouraging covered entities to do the same. *See* EO 322 at

pg. 9-10 (authorizing Commissioner of DOH to issue directives relating to reporting of COVID-19 vaccination data to DOH and ensuring private entities may keep policies and procedures implemented pursuant to EO 283).

The fact that these mandates were enacted by and on the judgment of a single person, and rescinded by and on the judgment of the same single person makes them substantially more capable of repetition than a legislative act, which requires bills to be introduced and to go through a public, lengthy, and deliberative process. These Mandates could be reenacted with no warning if the Governor, in his judgment, decided that new conditions warranted mandating the bivalent covid shot or any other medical procedure he believes will protect the public health. It is easier to repeat an action emanating from the singular judgment of an individual in the executive branch than it is to repeat an action that must go through the legislative process.

CONCLUSION

For the foregoing reasons, the Nurses petition this court to provide the meaningful relief of deciding their rights one way or another so they may plan their lives and careers accordingly.

Sincerely,

/s *Dana Wefer*

Dana Wefer, Esq.

Cc: All counsel by ECF

EXHIBIT A

96. Plaintiffs repeat and reallege each of the preceding paragraphs as if set forth fully herein.

97. Governor Philip Murphy has, while acting under the color and authority of law, deprived Plaintiffs of their constitutional rights.

PRAYER FOR RELIEF

Wherefore, Plaintiffs request the following relief:

98. Declare Executive Orders 283, 290 and 294 unconstitutional;

99. Declare Executive Order 283, 290, and 294 unconstitutional as applied to each Plaintiff;

100. Enjoin HMC and the State of New Jersey from enforcing the Mandate;

101. Grant Plaintiffs their costs and attorneys' fees under 42 U.S.C. Section 1988 and any other applicable authority; and

102. Grant any and all other such relief as this Court deems just and equitable.

Respectfully submitted,

Dated: April 18, 2022

s/ Dana Wefer, Esq.

Dana Wefer, Esq.
Attorney at Law

EXHIBIT B

American Pandemic Preparedness: Transforming Our Capabilities

September 2021

September 2, 2021

The Biden-Harris Administration is currently engaged in a whole-of-government review and update of U.S. national biopreparedness policies, as directed by the President in Executive Order 13987 and National Security Memorandum-1. This work will culminate in the release later this year of the Administration's strategy on biodefense and pandemic readiness.

As the President's American Jobs Plan stated, the United States has the opportunity and need to fundamentally transform our capabilities to protect the Nation. To ensure that the United States and the world are properly prepared, the work to develop those capabilities needs to begin now.

As a core element of the Administration's strategy on biodefense and pandemic readiness and informed by lessons from the COVID-19 pandemic, this document describes the critical work needed to transform U.S. capabilities to respond rapidly and effectively to any future pandemic or high consequence biological threat.

The work is organized across five pillars: (1) Transforming our Medical Defenses, (2) Ensuring Situational Awareness, (3) Strengthening Public Health Systems, (4) Building Core Capabilities, and (5) Managing the Mission.

Achieving these capabilities will require a systematic effort and shared vision for biological preparedness across our government that is akin to the nation's Apollo mission. The mission will require program management with the seriousness, commitment, and accountability of the Apollo Program, overseen by a dedicated program office.

Eric S. Lander
Assistant to the President for Science and Technology

Jacob J. Sullivan
Assistant to the President for National Security Affairs

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I. Introduction

Introduction

Protecting the United States from threats is a core responsibility of the Federal government. We have robust national defense capabilities that provide us with broad and deep protection against human threats, including missiles, terrorism, and cyberattacks. In the 21st century, we also need robust national biodefense capabilities that will provide us with broad and deep protection against biological threats, ranging from the ongoing and increasing risk of pandemic disease, to the possibility of laboratory accidents and the deliberate use of bioweapons.

The current pandemic has illustrated the seriousness of biological threats. As of mid-August 2021, COVID-19 has killed over 4.3 million globally, with excess-mortality estimates suggesting a death toll exceeding 10 million. In the United States, the number of deaths directly attributed to COVID-19 has surpassed 623,000, with many recovered patients living with long-term effects. The economic damage to the U.S. has been estimated at $16 trillion dollars in lost economic output, direct spending, mortality and morbidity[1]. And, the societal impact has been borne disproportionately by front-line and vulnerable populations, especially people of color.

As devastating as the COVID-19 pandemic is, there is a reasonable likelihood that another serious pandemic that may be worse than COVID-19 will occur soon — possibly within the next decade. Unless we make transformative investments in pandemic preparedness[2] now, we will not be meaningfully prepared.

1. Future biological threats could be far worse, and we are not adequately prepared

As staggering as the toll has been, future pandemics could be far worse.

• SARS-CoV-2, the virus responsible for COVID-19 disease, was favorable in certain respects. It is far less lethal than the 1918 influenza virus. It also belongs to a well-understood family: coronaviruses. It was possible to design vaccines within days of knowing the virus's genetic code because nearly 20 years of Federally-funded fundamental scientific research, spurred by the emergence of SARS and MERS, had provided detailed knowledge about coronaviruses, including revealing which protein to target and how to stabilize it. And while the current virus spins off variants, its mutation rate is slower than many viruses that have been studied. Unfortunately, most of the 26 families of viruses that infect humans are less well understood or harder to control than coronaviruses. While there are important lessons to be learned from COVID-19, we must not fall into the trap of preparing for yesterday's war.

The next pandemic will likely be substantially different from COVID-19. We must be prepared to deal with any viral threat.

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[1] *JAMA 2020; 324:1495–1496.*

[2] Pandemic "preparedness" and "readiness" are used synonymously.

• The development of mRNA vaccine technology and other 'programmable platforms'[3] — thanks to more than a decade of foresighted investment by the public and private sector — have been game-changing. mRNA vaccines shortened the time needed to design and test vaccines to a record-setting 314 days — far less than previous vaccines, which had taken several years. They have also been surprisingly effective against COVID-19. Still, there's so much we don't know about this vaccine platform, as well as other new platforms — including how they will perform against other types of viruses and how to optimize them.

Even with knowledge and tools that dramatically improved our ability to respond, COVID-19 has still been a catastrophe for the nation and the globe.

Conclusion: Before the next pandemic or other biological threat, we need to be able to respond to any possibility and to respond even faster and even better.

2. Serious biological threats will occur at an increasing frequency

Biological threats are increasing, whether naturally occurring, accidental, or deliberate, and the likelihood of a catastrophic biological event is similarly increasing.

Serious viral outbreaks have occurred frequently over the past century. Since the early 1900s, there have been at least 11 serious viral outbreaks, caused by pandemic pathogens which span five virus families (Table 1). Of those serious outbreaks, five have had lethality rates greater than or equal to COVID-19. In addition, many other new viruses have been emerging in recent decades.

Table 1. Serious Viral Outbreaks Over Past 100 Years

	Name	Virus Type	Year Began	Global Deaths	US. Deaths
1	**Spanish Flu**	Orthomyxovirus	1918	50,000,000	**675,000**
2	**Asian Flu (H2N2)**	Orthomyxovirus	1957	1,100,000	**116,000**
3	**Hong Kong Flu (H3N2)**	Orthomyxovirus	1968	1,000,000	**100,000**
4	**HIV**	Retrovirus	1981	32,700,000	**700,000**
5	**SARS-CoV-1**	Coronavirus	2002	774	
6	**Influenza (H1N1)**	Orthomyxovirus	2009	284,000	**12,469**
7	**MERS**	Coronavirus	2012	875	
8	**Ebola**	Filovirus	2014	11,310	**1**
9	**Zika**	Flavivirus	2015	N/A	
10	**Ebola**	Filovirus	2018	2,300	
11	**SARS-CoV-2**	Coronavirus	2019	4,100,000+	**621,000+**

There are compelling reasons to expect that the frequency will increase further in the years ahead:

[3] 'Programmable platforms' refer to technologies that can be easily adapted by inserting new genetic instructions.

• New infectious diseases have been emerging at a quickening pace due to increased zoonotic transmission from animals, driven by population growth, climate change, habitat loss, and human behavior, and these diseases are spreading faster with increased global travel.
• The number of laboratories around the world handling dangerous pathogens is growing in part as a response to increasing pandemic risk, boosting the likelihood that a contagious pathogen could be released accidentally.[4]
• As the technologies of modern biology become more powerful, affordable, and accessible, there is also the disturbing possibility that a malign actor could develop and use a biological weapon, including one that is highly contagious, in violation of the Biological Weapons Convention and UN Security Council Resolution 1540.

Conclusion: There will be an increasing frequency of natural — and possibly human-made — biological threats in the years ahead.

3. Pandemic Preparedness: Planning and Resources

For the first time in our history, we have the opportunity—due to advances in science and technology—not just to refill our stockpiles, but also to transform our capabilities. However, we need to start preparing now.

The United States must fundamentally transform its ability to prevent, detect, and rapidly respond to pandemics and high consequence biological threats. This would include investments in critical scientific goal areas—vaccines, therapeutics, diagnostics, and early warning—as well as associated investments in strengthening disease surveillance, health systems, surge capacity, personal protective equipment (PPE) innovation, biosafety and biosecurity, regulatory capacity, and global pandemic preparedness.

This document describes goals under five pillars:

I. **Transforming our Medical Defenses**, including dramatically improving vaccines, therapeutics, and diagnostics.
II. **Ensuring Situational Awareness** about infectious-disease threats, for both early warning and real-time monitoring.
III. **Strengthening Public Health Systems**, both in the U.S. and internationally to be able to respond to emergencies, with a particular focus on protecting the most vulnerable communities.
IV. **Building Core Capabilities**, including personal protective equipment, stockpiles and supply chains, biosafety and biosecurity, and regulatory improvement.
V. **Managing the Mission**, with the seriousness of purpose, commitment, and accountability of the Apollo Program.

The next section describes the goals and sub-goals. A separate Appendix provides scientific elaboration concerning the first pillar ('Transforming our Medical Defenses').

All of these efforts must, from the outset, include a strong emphasis on reducing inequities and increasing access by all Americans to the resulting advances.

[4] The 1977 H1N1 influenza pandemic killed ~700,000 people. Genomic evidence suggests it may have been caused by either a laboratory accident or botched vaccine trial (Rozo M and Gronvall G. mBio. 2015 6(4): e01013-15).

While the plan is focused on pandemic preparedness, the capabilities generated will also be extremely valuable for dealing with infectious disease in general — including improvements in vaccines, therapeutics, diagnostics, disease surveillance, public health, and regulation. Moreover, like previous ambitious scientific endeavors, the advances produced by this work will lead to broader benefits to human health.

Importantly, the COVID-19 pandemic has exposed fundamental issues with the Nation's public heath that go far beyond pandemic preparedness. These issues include the need to increase overall public health funding, strengthen the public health workforce, eliminate barriers to access, improve data systems, address disparities, improve communication, and improve coordination across Federal, state, local and Tribal authorities. This plan addresses needs directly related to pandemic preparedness, but the broader public health issues will need to be addressed separately in a concerted fashion.

This plan, aimed at transforming our capabilities, is a core element of the broader biodefense and pandemic preparedness strategy being developed by the Biden-Harris Administration, which will include updates to additional elements, policies, and practices.

Conclusion: We have the opportunity to transform our pandemic preparedness, and doing so will have major benefits for medical care and public health in ordinary times.

4. Pandemic Preparedness: Managing the Mission

The mission of transforming U.S. pandemic preparedness and biodefense capabilities should be managed with the seriousness of purpose, commitment, and accountability of an Apollo Program.

There should be a centralized 'Mission Control', acting as a single, unified program management unit, that draws on expertise from multiple HHS agencies, including NIH, CDC, BARDA, FDA, and CMS, as well as other departments such as DoD, DoE, and VA. (As an example, the Countermeasures Acceleration Group (formerly 'Operation Warp Speed') is led by a single joint program management unit.)

Mission Control should have the responsibility and authority to (i) develop and update plans with objective and transparent milestones; (ii) regularly assess and publicly report on mission progress; (iii) shift funding to ensure that goals are achieved; (iv) coordinate linkages across performers in government, academia, philanthropy, and industry; and (v) conduct periodic exercises to evaluate national pandemic preparedness by deploying national capabilities, including by rapid product development.

Mission Control should seek the input of outside experts on critical issues and consider establishing working group(s) that focus on scientific and technical assessments, improving public health and ensuring that the capabilities serve all communities, especially the most vulnerable.

5. Pandemic Preparedness: Cost and Economic Case

An effective program to ensure that the United States is prepared for future pandemics and other major biological threats will require significant annual investment over a sustained period.

However, the required investment is modest relative to other efforts to create the capabilities needed to protect the Nation against important threats: the annualized cost would be much smaller than what the U.S. spends on missile defense ($20 billion/year) and on preventing terrorism ($170 billion/year).

In addition to protecting American lives, the annual investment is strongly justified from an economic standpoint: If major pandemics similar to COVID-19, costing the U.S. roughly $16 trillion, occur at a frequency of every 20 years, the *annualized* economic impact on the U.S. would be $800 billion per year. **Even for somewhat milder pandemics, the *annualized* cost would likely exceed $500 billion.**

Conclusion:

Investing a modest amount annually to avert or mitigate the huge toll of future pandemics and other biological threats is an economic and moral imperative.

It's hard to imagine a higher economic — or human — return on national investment.

In any realistic accounting of costs and benefits, modest investments in pandemic preparedness should not be viewed as a cost, but instead as providing a large return on investment.

II. Goals

Goals

To be ready for the next pandemic, the United States will need to pursue goals in the five areas described below.

I. Transforming our Medical Defenses[5]

1. Vaccines

Goal: Have the ability to rapidly make effective vaccines against any virus family.

(1.1) Vaccine design, testing, and authorization. Enable design, testing, and review of a safe and effective vaccine against any human virus within 100 days after the recognition of a potential emerging pandemic threat.

(1.2) Vaccine production. Enable production of enough vaccine for the entire United States population within 130 days and for the global population within 200 days after its recognition as a potential emerging pandemic threat.

(1.3) Vaccine distribution. Enable delivery of vaccines rapidly and easily to anywhere in the world, by eliminating challenging requirements for transportation and storage, and enable distributed manufacturing.

(1.4) Vaccine administration. Enable rapid, large-scale vaccination campaigns, by simplifying vaccine administration — for example, replacing the need for sterile injection with skin patches and nasal sprays and the need for multiple doses with time-released formulation.

(1.5) Vaccine adaptation. Develop ways to rapidly adapt, test, and review modified vaccines to keep pace with changes in the virus.

2. Therapeutics

Goal: Have a range of therapeutics suitable for any virus family, available before a pandemic or readily created during a pandemic.

(2.1) Inhibiting key viral functions. Develop inhibitors that target essential viral functions, such as cell entry and replication, for any human viruses within a family or subfamily. (Effective inhibitors of this type have been developed for HIV and Hepatitis C.) Viral inhibitors would be valuable for treatment and prevention in both pandemic response and ordinary times (for example, to treat shingles or virally-caused meningitis). Promising approaches to develop anti-viral therapeutics include: (i) broadly-acting, small-molecule therapeutics against key viral functions, in advance of a pandemic and (ii) programmable RNA-based therapeutics targeted against specific viruses, for use during a pandemic.

[5] Acheiving the goals for 'Transforming Our Medical Defenses' will require extensive scientific and technological efforts, as outlined in the Scientific Appendix.

(2.2) Producing neutralizing antibodies against a virus. Develop, to deploy when a pandemic threat emerges, the ability to rapidly identify neutralizing antibodies in recovered patients and manufacture monoclonal antibodies for administration to infected individuals. While this approach is known to yield effective therapies for protecting infected individuals, we have lacked to ability to produce such antibodies at rapid-enough speed and large-enough scale for wide spread use.

(2.3) Controlling counterproductive patient responses to infection. Develop and characterize new therapeutics that limit damage from infectious diseases caused by over-or under-active responses of the human body to infection.

3. Diagnostics

Goal: Have simple, inexpensive, high-performance diagnostic tests available at large scale within weeks after the recognition of an emerging pandemic threat.

(3.1) Diagnostic test development. Develop diagnostic platforms for rapid, highly accurate tests that can be readily modified to respond to new and multiple pathogens and that can be deployed in a range of settings and use cases, including home, point of care, and central labs. Technologies should be inexpensive and accessible enough to meet national needs for frequent diagnostic testing, screening, and surveillance during sustained periods of high demand — including, if required, enabling daily home testing by an entire population to limit spread and direct medical care.

(3.2) Employ these diagnostics in public health. To ensure availability of diagnostic platforms in pandemic response, promote large-scale use of inexpensive, accessible, and reconfigurable testing platforms in medical care and public health in ordinary times, to enable routine testing for circulating viruses, including in home settings.

II. Ensuring Situational Awareness

4. Early-Warning Systems

Goal: Have the ability to detect viruses that pose a pandemic threat soon after they emerge in humans and produce and publicly share the full genome sequence.

(4.1) Viral threat detection in clinical settings. Incorporate into clinical care routine genome sequencing of samples from patients with unexplained fever or respiratory disease in the United States and abroad, in order to detect novel viral pathogens soon after they emerge. Expand capacity for genomic sequencing in clinical settings and data sharing, both domestically and internationally.

(4.2) Viral threat detection through environmental monitoring. Expand environmental sequencing, such as through wastewater sampling, in order to detect viruses closely related to known human pathogens circulating in communities, as a complement to viral threat detection in clinical settings.

(4.3) Aggregation of public health information. Create systems that connect real-time information about symptoms with genomic and other relevant public health information.

(4.4) Global early warning network. Support the establishment of a reliable global system for early warning of emerging pandemic threats. Enhance the effectiveness, interoperability, and connectivity of early threat detection at national and international levels with international partners.

5. Real-time Monitoring

Goal: When an emerging pandemic threat has been detected, have the ability to monitor the spread and evolution of the virus.

(5.1) Viral-infection monitoring. Enable effective monitoring, through various means, of virus spread in communities and large populations in order to inform public health response (by the integration of diagnostic, epidemiological, sequencing, environmental monitoring data).

(5.2) Tracking viral variants. As a virus spreads in communities, track changes in the genetic code of the virus and the potential impact of such changes on human health and effectiveness of vaccines, therapeutics, and diagnostics.

(5.3) Epidemic analysis and forecasting. Strengthen real-time analytics and develop accurate models to improve situational awareness and forecast the course of an outbreak, in order to inform communities and decision-makers about where to direct public health resources, bolster healthcare systems, deploy countermeasures, and communicate to the public. In support of this goal, examine and improve the quality of public health data streams.

III. Strengthening Public Health Systems

6. Strengthen the U.S. Public Health System by Expanding Capabilities to Respond to Public Health Emergencies

Goal: Modernize public health infrastructure, domestically and internationally, to effectively prevent, respond to, and contain biological threats.

(6.1) Strengthen the public health work force. Recruit and sustain a diverse cadre of public health experts at the local, state, and federal levels dedicated to preparing for and responding to public health emergencies, including teams that can be rapidly deployed internationally.

(6.2) Invest in public health laboratories and public health digital infrastructure. Ensure that public health labs have the capacity and infrastructure to detect, characterize, and report data (such as genome sequence and functional characterization) on pathogens safely and securely. In support of this, deploy a public health digital infrastructure, based on consistent data standards, which enables real-time data sharing and access across stakeholders involved in pandemic response as well as the public.

(6.3) Prioritize vulnerable communities. Develop strategies to mitigate the health inequities exacerbated during a public health emergency, including prioritizing allocation of public health emergency response resources – from public health workers assigned to communities to connectivity of clinical, data, and laboratory systems – to vulnerable and under-served communities.

(6.4) Support evidence-based public health communication. Support community engagement strategies, based in social science research, and involving community health workers, faith-based organizations, local leaders, and other community voices, to establish trusted communications channels for conveying critical public health information in preparation for and response to public health emergencies, including pandemics, and to bolster broader public health efforts.

7. Global Health Security Capacity to Support Pandemic Preparedness

Goal: Establish the international infrastructure and financing needed for pandemic preparedness.

(7.1) Local Capacity and International Systems. Create local capacity and international systems to optimally coordinate on R&D, clinical evaluation, product approval, and distribution of vaccines, therapeutics, diagnostics, and supplies.

(7.2) Sustainable financing. Catalyze sustainable international financing for health security capabilities for future pandemics and high consequence biological threats, including sustainable support for a global health security financing mechanism, such as a Financial Intermediary Fund, to support metrics-driven approaches to country capacity for countering biological threats.

IV. Building Core Capabilities

8. Personal Protective Equipment

Goal: Have effective, comfortable, and affordable Personal Protective Equipment (PPE).

(8.1) PPE Innovation. Develop solutions that increase the effectiveness, comfort, reusability, affordability, and manufacturability, including warm or surge capability, of PPE, to provide protection against pathogens with a range of properties.

(8.2) Pathogen protection within the built environment: Develop and deploy new technologies to improve indoor air quality, surface materials, and related aspects of transportation, buildings, and other infrastructure to suppress pathogen transmission among people. Invest in retrofitting high-risk infrastructure and incentivize private sector adoption of built environment pathogen suppression technologies for public protection.

9. Stockpiles and Supply Chains

Goal: Restore and expand the ability of the United States to produce the vital supplies to stop the next pandemic in its tracks.

(9.1) Refill stockpiles. Refill stockpiles that have been depleted by the current pandemic, to avoid near-term shortages while building longer-term onshore and near-shore manufacturing capacity for essential medical supplies.

(9.2) Build resilient supply chains. Ensure a stable and secure supply chain for key active ingredients for making vaccines, therapeutics, and diagnostics and for personal protective equipment.

10. Biosafety, Biosecurity, and Prevention of Catastrophic Biological Events

Goal: Prevent laboratory accidents and deter bioweapons development.

(10.1) Accelerate biosafety and biosecurity innovation. Expand capabilities to identify and minimize safety and security risks in the design and development in biotechnology, and share these tools globally.

(10.2) Ensure safe and secure R&D. Ensure R&D involving potentially dangerous biological agents is conducted safely and securely, by fostering a global research environment that adopts and enforces high standards.

(10.3) Deter and detect bioweapons development. Strengthen global norms against the development of pathogens as weapons, including by promoting international norms, transparency, and responsible scientific conduct. Strengthen oversight by developing better approaches to detect violations.

11. Regulatory Improvement

Goal: Improve regulatory capacity to support the development of safe and effective vaccines, therapeutics, and diagnostics.

(11.1) Regulatory approval for platforms. Improve regulatory systems, which typically focus on individual products, to be able to efficiently approve programmable platform technologies for vaccines, therapeutics, and diagnostics, in order to streamline the review of individual products that use these platforms.

(11.2) Clinical trial networks. Promote the development and operation of efficient, large-scale clinical trials networks in inter-pandemic times, with the ability to rapidly pivot to pandemic response. Design master protocols, ensure nationwide geographic coverage, train study coordinators to stand up sites quickly, include rural and community hospitals, and develop guidance for data collection and sharing.

(11.3) Regulatory capacity. Increase regulatory capacity and expand regulatory approaches at the FDA, in order to keep up with expanding needs in the years ahead.

V. Managing the Mission

12. Program Management

Goal: Manage this crucial national endeavor with the seriousness of purpose, commitment, and accountability of an Apollo Program and coordinate work with the international scientific community.

(12.1) U.S. Mission Control. Establish a strong, unified Mission Control to manage, integrate, and ensure accountability for all aspects of the U.S. pandemic preparedness program. Mission Control should have responsibility and authority to develop, update, and execute plans with objective and transparent milestones; regularly assess and report on mission progress, including by drawing on independent scientific panels; and conduct periodic exercises to evaluate national pandemic preparedness by deploying national capabilities, including by rapid product development.

(12.2) International Coordination. Galvanize global support and investment in international capabilities to contain pandemic threats wherever they emerge. Support the establishment of an international science and technology expert group to support and review progress toward global pandemic preparedness goals, including the 100 Day Mission.

III. Summary of Goals

Summary of Goals

This list provides a brief summary of the goals above.

I. Transform our Medical Defenses

1. Vaccines: Rapidly make effective vaccines against *any* human virus family
- Design, test, and review by 100 days after pandemic threat appears (for COVID-19 = May 2020)
- Produce enough vaccine for the U.S. by 130 days and entire world by 200 days
- Simplify vaccine distribution (e.g., eliminate need for cold storage)
- Simplify vaccine administration (e.g., replace sterile injection, with skin patches and nasal sprays)

2. Therapeutics: Life-saving medicines suitable for *any* virus family
- Develop medicines to block key virus functions (as done for HIV)
- Enable rapid production of neutralizing antibodies (currently too slow)
- Develop medicines to prevent severe immune over-reactions (useful in public health)

3. Diagnostics: Simple, inexpensive, accurate tests for *any* virus available within weeks
- Develop technologies to meet sustained demand, including daily home testing for all, if required
- Use new diagnostics in routine care, to serve public health, drive down costs, and expand capacity

II. Ensure Situational Awareness

4. Early-Warning Systems: Rapidly detect new viral outbreaks with pandemic potential
- Detect new threats by genome sequencing of patients with unexplained fevers in U.S. and abroad
- Detect new viral threats by wastewater sampling
- Create early-warning networks to aggregate and analyze global data

5. Real-time Monitoring: Follow existing viral outbreaks for spread and evolution
- Improve tracking by combining diagnostic, epidemiological, sequencing, and environmental data
- Improve analysis and forecasting

III. Strengthen Public Health Systems

6. U.S. Public Health. Modernize infrastructure to prevent and contain biological threats
- Strengthen the public health work force
- Invest in public health laboratories and public health digital infrastructure
- Prioritize vulnerable communities

7. Global Health. Establish international infrastructure and financing for pandemic preparedness
- Create local capacity and international systems
- Catalyze sustainable international financing

IV. Build Core Capabilities

8. Personal Protective Equipment. Increase effectiveness, comfort, affordability, and manufacturability

9. Stockpiles and Supply Chains. Ensure U.S. ability to produce vital supplies

10. Prevent Catastrophic Biological Events. Accelerate biosafety, biosecurity, and deterrence

11. Regulatory Improvement. Ensure regulatory capacity for vaccines, therapeutics, and diagnostics

V. Manage the Mission

12. Mission Control. Manage this national responsibility with the seriousness of purpose, commitment, and accountability of an Apollo Program and coordinate work with international scientific community

IV. Funding

Funding

The table below describes the total funding, above baseline, required to achieve the goals laid out in American Pandemic Preparedness: Transforming Our Capabilities. The total cost of the plan is $65.3 billion, to be invested over 7 to 10 years. (A portion of these funds are requested under the current budget reconciliation.)

It is critical that funds be appropriated to a single, unified "Mission Control" office at the Department of Health Human Services, responsible for overseeing the funds — in order to ensure the overall program management, execution, and accountability necessary to achieve the goals, as well as to enable close oversight by the White House and Congress.

Category	Funds ($B)
1. Vaccines	**$24.2**
1.1 Vaccine design, testing, and authorization, including testing of a range of candidate vaccines for all viral families and Phase III clinical trials for vaccines against active viral diseases	
1.2 Enable rapid, large-scale manufacturing capacity based on programmable platforms	
1.3 Simplify vaccine distribution, including by eliminating cold- chain transportation requirements	
1.4 Develop and test novel routes to simplify vaccine delivery and administration	
1.5 Adapt vaccines to keep pace with vaccine-defying variants	
2. Therapeutics	**$11.8**
2.1 Develop antivirals that inhibit key proteins for viral families, and evaluate in clinical trials against relevant diseases	
2.2 Ensure large-scale, programmable manufacturing capacity for monoclonal antibodies	
2.3 Develop host-specific therapeutics and immunomodulators, and evaluate in clinical trials	
3. Diagnostics	**$5.0**
3.1 Develop affordable and accessible diagnostics that can be deployed quickly at scale	
3.2 Expand diagnostic manufacturing capacity, by deploying new diagnostics in public health	
4. Early Warning	**$3.1**
4.1 Establish reliable clinical surveillance system for early detection of emerging pathogens	
4.2 Expand sequencing of pathogens circulating in communities, including in wastewater	
4.3 Aggregation and accessibility of relevant public health information, including clinical, epidemiological, and genome sequencing data	
4.4 Support establishment of a reliable, international early warning network	

5. Real-time Monitoring	**$2.3**
5.1 Enable effective monitoring of virus spread in communities, during a pandemic	
5.2 Enable effective tracking of virus evolution and its impacts on human health and vaccine efficacy	
5.3 Develop accurate models to forecast the course of an outbreak	
6. Strengthen the U.S. Public Health System by Expanding Capabilities to Respond to Public Health Emergencies	**$6.5**
6.1 Recruit and sustain a strong public health workforce dedicated to preparing for and responding to public health emergencies	
6.2 Strengthen public health lab infrastructure and capacity for pathogen detection, characterization, and reporting	
6.3 Reduce health inequities exacerbated by public health emergencies	
6.4 Support evidence-based public health communication	
7. Global Health Security Capacity to Support Pandemic Preparedness	**$2.8**
7.1 Strengthen local capacity and international systems for R&D, product approval, and rapid distribution of vaccines, therapeutics, diagnostics, and supplies	
7.2 Catalyze sustainable financing for health security capabilities for future pandemics and high consequence biological threats	
8. Personal Protective Equipment	**$3.1**
8.1 Promote next-generation PPE innovation	
8.2 Enhance pathogen protection in the built environment	
9. U.S. Capacity to Produce Vital Supplies	**$2.1**
9.1 Refill depleted pandemic stockpiles	
9.2 Build resilient supply chains, including for active pharmaceutical ingredients	
10. Strengthen Biosafety and Biosecurity, and Reduce Catastrophic Biological Threats	**$2.0**
10.1 Accelerate biosafety and biosecurity innovation	
10.2 Ensure safe and secure R&D	
10.3 Deter and detect biological weapons development and use	
11. Improve the Regulatory Environment	**$1.6**
11.1 Enable efficient regulatory approvals for platform technologies	
11.2 Create large, agile, and flexible clinical trials networks that can be rapidly ramped up for urgent needs	
11.3 Ensure regulatory capacity keeps pace with new technological developments	
12. Manage the Mission	**$0.8**
12.1 Establish Mission Control for pandemic preparedness	
12.2 Investment in international capabilities to contain pandemic threats where they emerge	
TOTAL AMOUNT NEEDED FOR MISSION (ABOVE BASELINE)	**$65.3**

[1] These estimates are preliminary and subject to change, depending on evolving agency assessments and ongoing agency consultations as part of the President's Budget process.

V. Scientific Appendix for Transforming our Medical Defenses

Scientific Appendix for Transforming our Medical Defenses

Preventing emerging infectious diseases from turning into devastating pandemics will require transforming our capabilities to produce vaccines that can protect against disease and block spread; therapeutics to prevent serious illness or death in infected individuals; and diagnostics to identify infected individuals in order to contain spread and target medical treatment.

With advances in science, we have the opportunity to develop scientific and technological capabilities that will not only help to prevent future pandemics, but will also provide broad public health benefits during inter-pandemic times. Importantly, we must be prepared for any type of virus, because the next potential pandemic may not resemble COVID-19.

This section serves as an appendix to American Pandemic Preparedness: Transforming Our Capabilities, providing scientific background concerning the plan's first pillar, on Transforming Our Medical Defenses.

Goal 1. Vaccines: Have the ability to rapidly make effective vaccines against any virus family.

(1.1) Vaccine design, testing, and approval. Design, test, and approve a safe and effective vaccine against any pathogenic human virus within 100 days following the identification of an emergent viral pandemic. While the 100-day target to produce vaccines for any virus is easy to state, achieving it will require an extensive scientific workplan:

- **Select one or more representative viruses for each virus family to characterize intensively ('prototype pathogens').** Success in quickly creating COVID-19 vaccines was possible only because of two decades of intense coronaviruses research that followed the 2002 SARS-CoV-1 outbreak in Asia. Since the next pandemic may not be caused by a coronavirus, we need to generate comparable information for all of the 26 families of viruses known to infect humans.
- **Leverage "programmable" platforms for rapid vaccine development.** New platforms for vaccine development, such as nucleic acid and recombinant viral vector technologies, are dramatically accelerating vaccine design by avoiding specialized, costly, and time-consuming steps of classical approaches. These platforms are at early stages: we should work to enhance these platforms and develop further new platforms.
- **Identify effective potential targets for design of vaccine candidates.** For each prototype pathogen, we will need to characterize viral protein structures, isolate antiviral antibodies, and identify the best viral targets for optimal vaccine design. In addition, we will need to define the extent of genetic variation and create virus family-specific tools and animal models that can be used for pre-clinical and clinical testing of vaccine candidates in animal models and humans.
- **Test the efficacy of dozens of candidate vaccines in animal models.** In animal studies, we will need to answer key questions for each virus family: Which viral proteins and specific sequences code for immunogens that generate the strongest immune responses? How well do vaccines perform against various targets? How much does vaccine safety and efficacy depend on how it is formulated?
- **Identify correlates/surrogates of protection in animal models.** Identifying correlates or surrogates of protection (such as the quantity and quality of neutralizing and other functional antibodies, as well as cellular responses), the tissues in which they are found, and the kinetics of

their appearance and persistence will aid in assessing the likely efficacy of human vaccine candidates.

- **Conduct small human clinical trials for many vaccine candidates to assess safety, likely efficacy based on correlates/surrogates of protection, and the impact of dose and schedule on immungenicity.** Small human research studies ("Phase 0") can show whether a vaccine candidate can elicit immune responses expected to mediate protection, although they won't directly test immune protection. (In the case of a highly transmissible and lethal threat from a pandemic or biological weapon, it is possible that biomarkers might need to serve as a substitute for direct protection.)
- **Test the effectiveness of vaccines developed against multiple targets and multiple genetic variants.** It will be important to assess the effectiveness of vaccines that target multiple viral proteins and/or genetic variants simultaneously. Such approaches might improve vaccine design in general, and might provide new ways to combat resilient and highly mutable viruses, like HIV and influenza, by encoding multiple targets in a single vaccine to generate broadly neutralizing antibodies and T-cell responses capable of broad-based protection.
- **Test the ability to develop 'universal vaccines' against all viruses in a family or subfamily.** A holy grail of vaccine research is creating vaccines that can protect against entire virus families, such as all coronaviruses or all influenza viruses, that mutate frequently and/or circulate seasonally. Programmable vaccine platforms will enable testing of multiple approaches to assess whether universal vaccines may be possible, with the potential to address entire families of viruses.
- **To enable the R&D work above, support the creation of biological foundries and pilot manufacturing plants to enable the design and production of many candidate vaccine design for clinical testing.** Access to excellent and efficient facilities for creating candidate vacines, using various programmable platforms, will streamline research and development. This includes foundries for cGMP synthesis of nucleic acids and proteins to serve as vaccine components and pilot-scale production lines to create cGMP vaccines for clinical testing.
- **Create infrastructure to enable rapid, large-scale clinical testing.** Vaccine trials involve administering vaccine or placebo to participants and waiting until a sufficient number of infections have occurred to determine if the vaccinated individuals show greater protection. Vaccine testing can be accelerating by increasing the size of the trial and by enrolling them rapidly. We will need robust, agile, and large-scale national and global clinical trials networks that can enroll many participants when needed. This should be a cooperative effort, involving public and private sponsors of clinical trial networks, standard-setting organizations such as the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, and global health leaders, such as the World Health Organization, to create interoperable clinical trial networks and sites that can be seamlessly pivoted towards pandemic response.
- **Develop effective clinical trial resources.** COVID-19 vaccine trials illustrated the importance of centralized, coordinated resources to support large-scale clinical trials. There needs to be a coordinated effort, established in advance, to proactively establish resources important to the conduct, review, and monitoring of clinical trials. This includes advance development of diverse and inclusive participant registries, master protocols, creation of centralized Institutional Review Boards and Data Safety Monitoring Boards, negotiated Reliance Agreements and Data Sharing/Use Agreements, development of data standards and standardized consent forms, and agreements on data repositories and intellectual property issues.

- **Apply technologies and standards to enable widely-distributed clinical trials.** Vaccine trials can be accelerated through decentralized clinical trial platforms that provide digital screening, remote enrollment, and remote patient monitoring (e.g., at-home sample collection, continuous physiological monitoring). Such approaches will improve quantitative outcome measures for trials for both efficacy and safety and will allow underserved populations to more readily participate.
- **Expanded regulatory capacity, vaccine safety monitoring, and post-market safety surveillance.** Vaccine trials that involves 100,000 participants may nonetheless not detect side effects that occur in only a tiny proportion of the population. As with any medical treatment, the only way to observe extremely rare risks is to continue to gather data once the vaccine is in use in the population. We must create and strengthen international safety monitoring networks to look for adverse events, including in low- and middle-income countries.

(1.2) Vaccine production. Enable production of enough vaccine for the entire U. S. population within 130 days and for the global population within 200 days after the recognition of a potential emerging pandemic threat.

- **To ensure that large-scale vaccine manufacturing capacity based on programmable platforms is available when pandemics emerge, ensure that such capacity is in active use for other purposes to serve regular medical and public health needs during inter-pandemic times.** It is not feasible to maintain idle factories that are be taken out of mothballs when pandemics strike. Rather, it is will be important to have "hot" manufacturing capacity in continuous use during inter-pandemic times (producing vaccines against infectious diseases, as well as possibly other products, such as cancer vaccines) that can be redirected for pandemic response.
- **To ensure that there is sufficient capacity to vaccinate the world, develop and simplify methods that decrease the material required for effective vaccination.** It is critical to have the ability to rapidly produce enough vaccine to supply the world. At present, producing 20 billion doses in Pfizer-BioNtech's five manufacturing facilities would require about three years. However, if the dosage could be reduced by ten-fold, the time could be slashed to under four months. Efforts should be undertaken to define dosage-response relationships in animals (based on protection) and humans (using predictors of protection) and to increase the vaccine potency—for example, via adjuvants, delivery mechanisms and, in the case of mRNA vaccines, approaches such as self-amplifying RNA.

(1.3) Vaccine distribution. Enable delivery of vaccines rapidly and easily to anywhere in the world, by eliminating challenging requirements for transportation and storage.

- **Simplify vaccine distribution and delivery, including by eliminating the need for cold chain.** Vaccine formulations that do not require specialized conditions, such as ultra-cold temperatures, and are long-lived will simplify transportation to both resource-rich and resource-constrained settings around the world.

(1.4) Vaccine administration. Enable rapid, large-scale vaccination campaigns, by simplifying vaccine administration — for example, replacing the need for sterile injection with skin patches and nasal sprays and the need for multiple doses with time-released formulation.

- **Simplify vaccine administration so that vaccines can be safely administered by minimally-trained personnel**. Needle-free vaccine delivery methods, such as nasal sprays or microneedle skin patches, could reduce or eliminate the need for specialized health personnel to administer

vaccines. Multi-dose vaccines might be delivered in a single administration by using timed-release formulations.

(1.5) Vaccine adaptation. Develop ways to quickly and easily update vaccines to keep pace with changes in the virus.

- **Develop strategies to address viral variants that evade vaccine-induced immunity.** As virus spreads, they will likely evolve the ability to increase their transmissibility — including in vaccinated individuals. Efforts should be undertaken now to understand the relative effectiveness of various strategies for dealing with vaccine evasion, including using boosters to increase antibody titer and administering 'next-generation' of vaccines matched to variant strains.

Goal 2. Therapeutics: Have a range of therapeutics suitable for any virus family, available before a pandemic or readily created during a pandemic.

(2.1) Inhibiting key viral functions. Develop inhibitors that target essential viral functions, such as cell entry and replication, for any human viruses within a family or subfamily. (Effective inhibitors of this type have been developed for HIV and Hepatitis C.) Viral inhibitors would be valuable for treatment and prevention in both pandemic response and ordinary times (for example, to treat shingles or virally-caused meningitis). Promising approaches to develop anti-viral therapeutics include:

- **Develop broadly-acting small-molecule therapeutics against key viral functions, in advance of a pandemic.** Development of small-molecule therapeutics against viral proteins, such as polymerases or proteases, is a well-established approach — involving high-throughput screening using in vitro or cellular systems to identify molecules, chemical optimization to produce lead molecules, preclinical testing, and clinical testing. Because the approach is too slow to enable creation of new therapeutics in the midst of a pandemic, it is necessary to identify and test broadly-acting therapeutics against viral families in advance of a pandemic. The goal would be to develop therapeutics that are effective across a broad spectrum of viruses within a viral family or across multiple viral families.
- **Develop the ability to rapidly create programmable RNA-based therapeutics targeted against specific viruses, for use during a pandemic response.** Programmable RNA-based therapeutics, in which pathogen sequences are inserted into an existing platform, may enable rapid development of therapeutics against specific viruses — for example, to block viral replication, entry into cells, or other key functions. (These technologies include short interfering RNAs (siRNAs), antisense oligonucleotides, and CRISPR-based approaches. For example, siRNA is currently being developed as a possible treatment for Hepatitis B.) Developing these platforms now to treat existing viral infections would develop the knowledge base and capacity to use programmable RNA therapeutics to rapidly respond to a novel pathogen.

(2.2) Producing neutralizing antibodies against a virus. Develop, to deploy when a pandemic threat emerges, the ability to rapidly identify neutralizing antibodies in recovered patients and manufacture monoclonal antibodies for administration to infected individuals. While this approach is known to yield effective therapies for protecting infected individuals, we have lacked to ability to produce such antibodies at rapid-enough speed and large-enough scale for wide spread use.

- **Ensure large-scale programmable manufacturing capacity for monoclonal antibodies.** Continued efforts are needed to optimize the process for identifying and selecting neutralizing antibodies, and to design manufacturing processes for large-scale antibody production.

Opportunities exist to expand the use of monoclonal antibodies in clinical care for chikungunya and other known viruses during inter-pandemic periods to offer the first targeted. As with vaccine production, it is will be important to have "hot" manufacturing capacity in continuous use during inter-pandemic times (producing antibodies against infectious diseases, as well as possibly other products) that can be redirected for pandemic response.

(2.3) Controlling counterproductive patient responses to infection. Develop and characterize new therapeutics that limit damage from infectious diseases caused by over-or under-active responses of the human body to infection.

- **Develop therapeutics to modulate responses by the immune, circulatory, and other organ systems to viral infection.** Modulators of the immune system—such as dexamethasone and tocilizumab, which act through distinct mechanisms—were found to reduce mortality among the sickest COVID-19 patients. Therapeutics targeting the respiratory system or the circulatory system would be useful for treatment of pneumonia or blood clotting symptoms in both ordinary times and during pandemic response.

Goal 3. Diagnostics: Have simple, inexpensive high-performance diagnostic tests available at large scale within weeks after the recognition of an emerging pandemic threat.

(3.1) Diagnostic test development. Develop diagnostic platforms for rapid, highly accurate tests that can be readily modified to respond to new and multiple pathogens and that can be deployed in a range of settings and use cases, including home, point of care, and central labs. Technologies should be affordable and accessible enough to meet national needs for frequent diagnostic testing, screening, and surveillance during sustained periods of high demand — including, if needed, enabling daily home use by an entire population, to limit spread and direct medical care.

- **Develop viral-specific, rapid-turnaround tests that can be self-administered in any environment.** We promote innovation in diagnostic testing, by supporting the design, development, and deployment of programmable platforms with the potential to be highly accurate, extremely inexpensive, easy to use, readily accessible, and rapidly manufactured. In addition, manufacturing capacity needs to be maintained in inter-pandemic times, and raw materials need to be available immediately at the onset of a pandemic. There are opportunities with respect to the analyte detected (nucleic acids, proteins), sampling strategies (nasal swabs, saliva or exhaled breath), analytical chemistries, and integration with mobile devices. We also need to ensure that tests can be reconfigured within two weeks of the detection of a potential pandemic threat.

(3.2) Employ these diagnostics in public health. Develop and produce innovative test platforms for routine diagnosis, screening, and surveillance of existing infectious and chronic diseases in patients today, while ensuring the ability to rapidly reconfigure them to detect new pathogens and threats in future pandemics.

- **Integrate rapid diagnostics into current point-of-care treatment.** Diagnostic tests that cost pennies and yield results in minutes could speed patient triage in emergency rooms, extend diagnostics into primary care settings, and be used for home testing together with telehealth. These diagnostic tests would have immediate benefit for diagnosing and treating influenza, human respiratory syncytial virus, antibiotic-resistant bacterial infections, and many other infectious diseases.