

DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, EDUCATION, AND RELATED AGENCIES  
APPROPRIATIONS FOR 2022

HEARINGS  
BEFORE A  
SUBCOMMITTEE OF THE  
COMMITTEE ON APPROPRIATIONS  
HOUSE OF REPRESENTATIVES  
ONE HUNDRED SEVENTEENTH CONGRESS  
FIRST SESSION

SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN SERVICES,  
EDUCATION, AND RELATED AGENCIES

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**DEPARTMENTS OF LABOR, HEALTH AND  
HUMAN SERVICES, EDUCATION, AND RE-  
LATED AGENCIES APPROPRIATIONS FOR  
2022**

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TUESDAY, MAY 25, 2021.

**NATIONAL INSTITUTES OF HEALTH**

**WITNESSES**

**FRANCIS S. COLLINS, M.D., DIRECTOR, NATIONAL INSTITUTES OF  
HEALTH**

**DIANA W. BIANCHI, M.D., DIRECTOR, EUNICE KENNEDY SHRIVER NA-  
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**NORMAN E. SHARPLESS, M.D., DIRECTOR, NATIONAL CANCER INSTI-  
TUTE**

**NORA D. VOLKOW, M.D., DIRECTOR, NATIONAL INSTITUTE ON DRUG  
ABUSE**

The CHAIR. This hearing will come to order.

As this hearing is fully virtual, we must address a few house-keeping matters.

For today's meeting, the Chair or staff designated by the Chair may mute participants' microphones when they are not under recognition for the purposes of eliminating inadvertent background noise.

Members are responsible for muting and unmuting themselves. If I notice that you have not unmuted yourself, I will ask you if you would like the staff to unmute you. If you indicate approval by nodding, staff will unmute your microphone.

I remind all members and witnesses that the 5-minute clock still applies. If there is a technology issue, we will move to the next member until the issue is resolved, and you will retain the balance of your time.

You will notice a clock on your screen that will show how much time is remaining. At 1 minute remaining, the clock will turn yellow. At 30 seconds remaining, I will gently tap the gavel to remind members that their time is almost expired. When your time has expired, the clock will turn red, and I will begin to recognize the next member.

In terms of the speaking order, we will begin with the chair and ranking member. Then members present at the time the hearing is called to order will be recognized in order of their seniority, and

finally, members not present at the time the hearing is called to order.

Finally, House rules require me to remind you that we have set up an email address to which members can send anything they wish to submit in writing at any of our hearings or markups. That email address has been provided in advance to your staff.

And with that, I want to acknowledge Ranking Member Cole and all of our colleagues for joining this morning, and I want to thank our witnesses for testifying.

Good morning to Dr. Collins. Welcome back to the Labor, HHS, Education Appropriations Subcommittee.

I would also like to welcome the five institute directors joining Dr. Collins today: Dr. Diana Bianchi, Director of the Eunice Kennedy Shriver National Institute of Child Health and Human Development; Dr. Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases; Dr. Gary Gibbons, Director of the National Heart, Lung, and Blood Institute; Dr. Ned Sharpless, Director of the National Cancer Institute; and Dr. Nora Volkow, Director of the National Institute on Drug Abuse.

I want to note that I intend to invite an additional panel of institute and center directors to testify in front of the subcommittee later this year. We were not able to hold a second panel last year due to the pandemic, but I want to make sure the subcommittee hears from every institute about its promising research.

The last time Dr. Collins and the IC directors were here to testify on the National Institutes of Health budget was March 4, 2020. There were 128 newly reported COVID cases that day in the United States, which more than doubled the total number of cases that had been identified to date.

Later that day, the House would pass the first COVID supplemental bill, which included over \$800 million to support NIH on basic research, diagnostics, treatments, and vaccines for COVID-19.

Today, over 14 months later, the Congress has provided over \$4.8 billion to support NIH research related to COVID.

Based in part on these investments and the partnerships with other agencies and the private sector, three COVID-19 vaccines were developed in record time and are now widely available in the United States, and nearly 300 million vaccine doses have been administered, including nearly 4 million in my home State of Connecticut.

In my view, this is a remarkable achievement made possible not only by targeted investment in COVID research, but also by the annual sustained investment in biomedical research made by this committee in recent years.

In the 20 years before the COVID-19 pandemic, the National Institute of Allergy and Infectious Diseases, NIAID, invested over \$650 million in basic research on coronavirus, and in particular on the spike protein that is the target of coronavirus vaccines. This crucial breakthrough allowed researchers at the NIAID Vaccine Research Center to rapidly generate a stabilized spike protein for use in developing the COVID-19 vaccines in use today.

In addition, NIH has also made substantial investments into mRNA technology and its potential use in vaccines and thera-



peutics, which was essential to the rapid development of COVID vaccines.

I call your attention to an article that was November of 2020, and I will just give you the title: “Government-Funded Scientists Laid the Groundwork for Billion-Dollar Vaccines.” And I mention this because I think it is critical in what this committee is able to accomplish and also what our scientists at the NIH, with the funds, Federal funds, are able to accomplish.

Quite frankly, it is such a relief to millions of Americans to finally have access to the COVID vaccine.

In Connecticut a couple of weeks ago we had a FEMA mobile vaccination clinic open on the New Haven Green. A family with two teenagers was there to get their vaccines. Their father, Roberto, said that he wanted his daughter, Sophia, and his son, Diego, to get vaccinated as soon as possible to avoid the risk of their contracting COVID and spreading it to the youngest of their younger sisters, who is only 4 years old.

After receiving her shot, Sophia, who is 16, said, and I quote, “Now I am vaccinated. It means I won’t be afraid to get COVID–19 as much as I was before,” end quote.

Can you imagine being a 16-year-old and fearing for your life and the health of your family? Thanks to the vaccine, Sophia and her brother can finally stop living in fear and get back to being normal teenagers.

This is just one of the many stories of how the COVID vaccine has made such an immeasurable difference in our lives.

None of it would have been possible without the increased funding that Congress has consistently provided for the NIH. And I am proud that we have increased NIH funding by \$12.9 billion, 42 percent, over the past 6 years. And this support has been bipartisan from this subcommittee. Last year, the Congress provided an additional \$1.25 billion increase over the fiscal year 2020 level for the NIH.

I am pleased to see President Biden’s budget request to continue the momentum in fiscal year 2022. The request proposes an increase of about \$2.5 billion to expand funding for NIH’s core activities, such as research grants, clinical trials, and infrastructure support. The request also proposes to establish a new Advanced Research Projects Agency for Health, or ARPA–H, to accelerate the development of treatments and cures.

I am especially glad to see that the budget proposes increased investment in research on maternal health to address the crisis of maternal mortality. In the U.S., maternal mortality is such a major problem and an issue that I have been working on for quite some time, as have so many of my colleagues.

I also look forward to further details about how the budget proposal will support research on how to reduce racial and ethnic disparities in maternal health outcomes and improve maternal mental health.

In that vein, I am grateful that this budget proposes increased funding for research into other health and mental health disparities that are disproportionately affecting underrepresented communities.

As I have often said, these issues have been further exposed and exacerbated by the COVID-19 pandemic. And as Dr. Collins says so eloquently in his written testimony, it is, and I quote, “forcing a recognition that our country is still suffering the consequences of centuries of racism.”

I was also glad to see that the budget doubles funding for research on gun violence prevention at the NIH, building off the investments the subcommittee has made over the past 2 years. I am interested in getting a progress report on the funded projects and any potential evaluation that you may have. I know it may be too early, but I hope you can let us know a little more about the status of this program.

I might add that I am intrigued by the proposal to establish ARPA-H as it appears to be a novel approach to supporting innovation to address problems in health and medical research. I look forward to learning more about this proposal.

And I want to emphasize that it is critical that we strike a balance between this new approach and investments in basic research and fundamental discovery at NIH.

As I noted earlier, the Congress and this subcommittee have consistently provided funding for basic research at NIH that was integral in setting the stage for the rapid development of COVID-19 vaccines.

As we move forward, I think it will be important to balance the promise of this new approach with a continued commitment to basic research.

One of my priorities on a Labor-HHS bill has been to ensure a strong across-the-board increase for NIH research so that we continue to invest in all areas of research instead of limiting new investments to a few of the most high profile diseases.

I am disappointed that research on amyotrophic lateral sclerosis, ALS, has not been mentioned as a potential area of focus for ARPA-H and hope to learn more about how NIH proposes to make decisions about how best to target ARPA-H funding.

I am also curious to hear more about how ARPA-H would differ from existing NIH centers and programs that support high risk, high reward research, such as the National Center for Advancing Translational Sciences, NCATS.

I realize that because the administration’s full budget has not yet been released, Dr. Collins, you cannot provide all of the details on the NIH request today. But I believe we can have a good discussion on the priorities that have been announced, and we look forward to receiving the full NIH request in a few days.

Now let me turn to my friend from Oklahoma, the ranking member, Congressman Cole, for any opening remarks that he may have.

Mr. COLE. Well, thank you very much, Madam Chair. And I could probably just say “amen” and dispense with my remarks because there is essentially nothing in your opening statement that I don’t agree with wholeheartedly.

I have enjoyed all the hearings held by the subcommittee this year, and that is a compliment to you, Madam Chair. I think we have had a succession of really terrific hearings on a variety of topics.

But, I must admit, welcoming the scientific leaders from the National Institutes of Health is the hearing I most look forward to every year.

I am pleased to once again welcome Director Francis Collins. As I often say, clearly the best politician in Washington, DC, having been appointed by President Obama, President Trump, and now President Biden. I challenge anybody to match that record. But I think it is a clear indication of how much regard the Director is held in, and, frankly, the NIH itself.

Each year brings new and exciting innovations in medicine and treatment and a glimpse into the world and the possibilities of our future. I am always encouraged when we learn about these scientific advancements.

And I know I have said this numerous times, but it bears repeating: Increasing funding for the NIH is one of the best bipartisan accomplishments of this subcommittee, Madam Chair, as you noted in your opening statement.

Let me break from my prepared statement to make a point that I think is important to make here.

I have made the point repeatedly in previous hearings that I think the administration's budget is pretty heavy on domestic spending, it goes up 18 percent, pretty light on defense spending, which is flat and actually has an inflation adjusted cut. And I have said that that needs to change, that the defense number needs to come up and the domestic number, in my opinion, needs to come down, or we run the risk of a CR.

Having said that, I want to make it crystal clear, I support the President's topline budget number for the NIH, and I would throw in the CDC and the Strategic Stockpile as well. I think those are areas of critical national investment that we can all work together on and see the benefit of.

And I say that just to make it clear to my friends, while I haven't changed my view on the overall budget in this area, I doubt there is much daylight between the chairman and me as to the importance of this investment for our future. I think we have demonstrated that together over the last 6 years. I am comfortable and confident we will demonstrate that again going forward.

The sustained commitment to increasing funding for the NIH is a vital step in preserving our status as the world's leader in biomedical research and to finding novel treatments and cures for the many diseases burdening our strained healthcare system.

The funding also does far more. Several studies have shown funding for the NIH has a multiplier effect, contributing to overall U.S. economic growth.

The investments made at NIH over the past few years, and, even further back, over the past decades, as our chair pointed out, laid the groundwork for our response to the COVID pandemic.

The National Cancer Institute stepped in with advanced lab capacity.

The National Institute of Allergy and Infectious Diseases led the way with expertise related to infectious disease.

The Office of the Director supported efforts to make rapid advancements in therapeutics and diagnostics.

And of course, last but certainly not least, with NIH support, Operation Warp Speed provided enough doses of vaccine for every adult in America.

The NIH is a shining example of what can be achieved when we put our best minds together and work to accomplish bold and challenging goals.

Much attention in the past year has gone to COVID and the associated scientific discoveries, and rightly so. But I hope in the coming years we can also continue our conversations and scientific advancements in Alzheimer's disease and cancer treatment.

These two areas have seen strong congressional interest and represent a foundational shift in how we treat diseases responsible for the loss of most Americans each year.

I also hope that the promises of precision medicine can be experienced by more patients and believe that the All Of Us Program can improve how we use genetic information in routine medical care.

Dr. Collins, you have once again brought an excellent team representing some of the largest institutes and most promising frontiers of new discoveries. I look forward to hearing from all of you.

I also want to recognize that the NIH is composed of 27 institutes and centers, most of whom are not able to be with us today. Even though we are not able to have each director come before us, our offices continuously hear about the groundbreaking work and collaborative partnerships at all of the NIH components. We know that work is done across the NIH and that each institute or center is a contributor.

In closing, I want to stress that each dollar invested in the NIH is a down payment on our future. This work has in the past, and will in the future, continue to improve the course of disease detection, treatment, and even cures in the years and generations to come. I know congressional commitment to advancing these shared objectives has been unwavering.

And I want to thank you, Madam Chair, for holding the hearing. And, frankly, more importantly, thank you for your long record of support for the NIH and dealing with the issues of disease. It has been an area where you have led throughout your career, and you continue to lead today. And you certainly have all of our support on this committee in that effort.

With that, Madam Chair, I yield back.

The CHAIR. Thank you for your comments, but again, most importantly, the friendship, but working together on this issue, which is so critically important. And it has been really a team effort, and I am most appreciative of that.

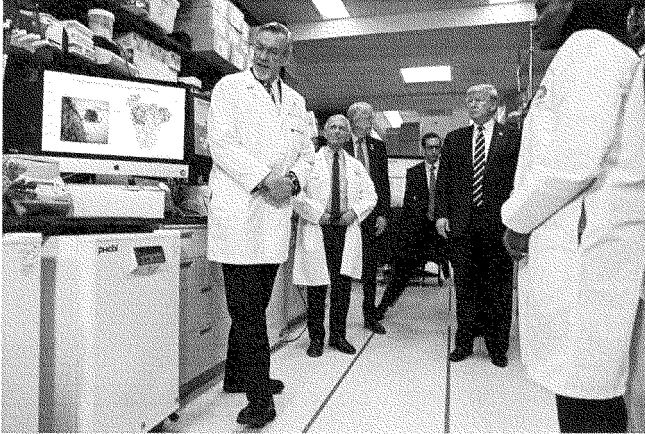
Before I turn to Dr. Collins, I want to ask unanimous consent to put into the record the article I referenced, "Government-Funded Scientists Laid the Groundwork for Billion-Dollar Vaccines."

[The information follows:]

COVID-19

## Government-Funded Scientists Laid the Groundwork for Billion-Dollar Vaccines

By Arthur Allen • NOVEMBER 18, 2020



Dr. Barney Graham, deputy director at the Vaccine Research Center at the National Institutes of Health, gives President Donald Trump a tour of the Viral Pathogenesis Laboratory at NIH on March 3 in Bethesda, Maryland. (AP Photo/Evan Vucci)

When he started researching a troublesome childhood infection nearly four decades ago, virologist Dr. Barney Graham, then at Vanderbilt University, had no inkling his federally funded work might be key to deliverance from a global pandemic.

Yet nearly all the vaccines advancing toward possible FDA approval this fall or winter are based on a design developed by Graham and his colleagues, a concept that emerged from a scientific quest to understand a disastrous 1966 vaccine trial.

Basic research conducted by Graham and others at the National Institutes of Health,

Defense Department and federally funded academic laboratories has been the essential ingredient in the rapid development of vaccines in response to COVID-19. The government has poured an additional \$10.5 billion into vaccine companies since the pandemic began to accelerate the delivery of their products.

The Moderna vaccine, whose remarkable effectiveness in a late-stage trial was announced Monday morning, emerged directly out of a partnership between Moderna and Graham's NIH laboratory.

Coronavirus vaccines are likely to be worth billions to the drug industry if they prove safe and effective. As many as 14 billion vaccines would be required to immunize everyone in the world against COVID-19. If, as many scientists anticipate, vaccine-produced immunity wanes, billions more doses could be sold as booster shots in years to come. And the technology and production laboratories seeded with the help of all this federal largesse could give rise to other profitable vaccines and drugs.

The vaccines made by Pfizer and Moderna, which are likely to be the first to win FDA approval, in particular rely heavily on two fundamental discoveries that emerged from federally funded research: the viral protein designed by Graham and his colleagues, and the concept of RNA modification, first developed by [Drew Weissman](#) and [Katalin Karikó](#) at the University of Pennsylvania. In fact, Moderna's founders in 2010 named the company after this concept: "Modified" + "RNA" = Moderna, according to [co-founder Robert Langer](#).

"This is the people's vaccine," said corporate critic Peter Maybarduk, director of Public Citizen's Access to Medicines program. "Federal scientists helped invent it and taxpayers are funding its development. ... It should belong to humanity."

Moderna, through spokesperson Ray Jordan, acknowledged its partnership with NIH throughout the COVID-19 development process and earlier. Pfizer spokesperson Jerica Pitts noted the company had not received development and manufacturing support from the U.S. government, unlike Moderna and other companies.

The idea of creating a vaccine with messenger RNA, or mRNA — the substance that converts DNA into proteins — goes back decades. Early efforts to create mRNA vaccines failed, however, because the raw RNA was destroyed before it could generate the desired response. Our innate immune systems evolved to kill RNA strands because that's what many viruses are.

Karikó came up with the idea of modifying the elements of RNA to enable it to slip past the immune system undetected. The modifications she and Weissman developed allowed RNA to become a promising delivery system for both vaccines and drugs. To be sure, their work was enhanced by scientists at Moderna, BioNTech and other laboratories over the past decade.

Another key element in the mRNA vaccine is the lipid nanoparticle — a tiny, ingeniously designed bit of fat that encloses the RNA in a sort of invisibility cloak, ferrying it safely through the blood and into cells and then dissolving, thereby allowing the RNA to do its work of coding a protein that will serve as the vaccine's main active ingredient. The idea of enclosing drugs or vaccines in lipid nanoparticles arose first in the 1960s and was developed by Langer and others at the Massachusetts Institute of Technology and various academic and industry laboratories.

Karikó began investigating RNA in 1978 in her native Hungary and wrote her first NIH grant proposal to use mRNA as a therapeutic in 1989. She and Weissman achieved successes starting in 2004, but the path to recognition was often discouraging.

"I keep writing and doing experiments, things are getting better and better, but I never get any money for the work," she recalled in an interview. "The critics said it will never be a drug. When I did these discoveries, my salary was lower than the technicians working next to me."

Eventually, the University of Pennsylvania sublicensed the patent to Cellscript, a biotech company in Wisconsin, much to the dismay of Weissman and Karikó, who had started their own company to try to commercialize the discovery. Moderna and BioNTech later would each pay \$75 million to Cellscript for the RNA modification patent, Karikó said. Though unhappy with her treatment at Penn, she remained there until 2013 — partly because her daughter, Susan Francia, was making a name for herself on the school's rowing team. Francia would go on to win two Olympic gold medals in the sport. Karikó is now a senior officer at BioNTech.

In addition to RNA modification and the lipid nanoparticle, the third key contribution to the mRNA vaccines — as well as those made by Novavax, Sanofi and Johnson & Johnson — is the bioengineered protein developed by Graham and his collaborators. It has proved in tests so far to elicit an immune response that could

prevent the virus from causing infections and disease.

The protein design was based on the observation that so-called fusion proteins — the pieces of the virus that enable it to invade a cell — are shape-shifters, presenting different surfaces to the immune system after the virus fuses with and infects cells. Graham and his colleagues learned that antibodies against the post-fusion protein are far less effective at stopping an infection.

The discovery arose in part through Graham's studies of a 54-year-old tragedy — the failed 1966 trial of an NIH vaccine against respiratory syncytial virus, or RSV. In a clinical trial, not only did that vaccine fail to protect against the common childhood disease, but most of the 21 children who received it were hospitalized with acute allergic reactions, and two died.

About a decade ago, Graham, now deputy director of NIH's Vaccine Research Center, took a new stab at the RSV problem with a postdoctoral fellow, Jason McLellan. After isolating and obtaining three-dimensional models of the RSV's fusion protein, they worked with Chinese scientists to identify an appropriate neutralizing antibody against it.

"We were sitting in Xiamen, China, when Jason got the first image up on his laptop, and I was like, oh my God, it's coming together," Graham recalled. The prefusion antibodies they discovered were 16 times more potent than the post-fusion form contained in the faulty 1960s vaccine.

Two 2013 papers the team published in *Science* earned them a runner-up prize in the prestigious journal's Breakthrough of the Year award. Their papers, which showed it was possible to plan and create a vaccine at the microscopic structural level, set the NIH's Vaccine Research Center on a path toward creating a generalizable, rapid way to design vaccines against emerging pandemic viruses, Graham said.

In 2016, Graham, McLellan and other scientists, including Andrew Ward at the Scripps Research Institute, advanced their concept further by publishing the prefusion structure of a coronavirus that causes the common cold and a patent was filed for its design by NIH, Scripps and Dartmouth — where McLellan had set up his own lab, NIH and the University of Texas — where McLellan now works — filed an additional patent this year for a similar design change in the virus that causes



## COVID-19.

Graham's NIH lab, meanwhile, had started working with Moderna in 2017 to design a rapid manufacturing system for vaccines. In January, they were preparing a demonstration project, a clinical trial to test whether Graham's protein design and Moderna's mRNA platform could be used to create a vaccine against Nipah, a deadly virus spread by bats in Asia.

Their plans changed rapidly when they learned on Jan. 7 that the epidemic of respiratory disease in China was being caused by a coronavirus.

"We agreed immediately that the demonstration project would focus on this virus" instead of Nipah, Graham said. Moderna produced a vaccine within six weeks. The first patient was vaccinated in an NIH-led clinical study on March 16; early results from Moderna's 30,000-volunteer late-stage trial showed it was nearly 95% effective at preventing COVID-19.

Although other scientists have advanced proposals for what may be even more potent vaccine antigens, Graham is confident that carefully designed vaccines using nucleic acids like RNA reflect the future of new vaccines. Already, two major drug companies are doing advanced clinical trials for RSV vaccines based on the designs his lab discovered, he said.

In a larger sense, the pandemic could be the event that paves the way for better, perhaps cheaper and more plentiful vaccines.

"It's a silver lining, but I think we are definitely pushing forward the way everyone is thinking about vaccines," said Michael Farzan, chair of the department of immunology and microbiology at Scripps Research's Florida campus. "Certain techniques that have been waiting in the wings, under development but never achieving the kind of funding they needed for major tests, will finally get their chance to shine."

Under a 1980 law, the NIH will obtain no money from the coronavirus vaccine patent. How much money will eventually go to the discoverers or their institutions isn't clear. Any existing licensing agreements haven't been publicized; patent disputes among some of the companies will likely last years. HHS' big contracts with the vaccine companies are not transparent, and Freedom of Information Act requests have been

slow-walked and heavily redacted, said Duke University law professor Arti Rai.

Some basic scientists involved in the enterprise seem to accept the potentially lopsided financial rewards.

"Having public-private partnerships is how things get done," Graham said. "During this crisis, everything is focused on how can we do the best we can as fast as we can for the public health. All this other stuff is going to have to be figured out later."

"It's not a good look to become extremely wealthy off a pandemic," McLellan said, noting the big stock sales by some vaccine company executives after they received hundreds of millions of dollars in government assistance. Still, "the companies should be able to make some money."

For Graham, the lesson of the coronavirus vaccine response is that a few billion dollars a year spent on additional basic research could prevent a thousand times as much loss in death, illness and economic destruction.

"Basic research informs what we do, and planning and preparedness can make such a difference in how we get ahead of these epidemics," he said.

*This story was produced by KHN, which publishes California Healthline, an editorially independent service of the California Health Care Foundation.*

Arthur Allen: [ArthurA@kff.org](mailto:ArthurA@kff.org), [@ArthurAllen202](https://twitter.com/ArthurAllen202)

The CHAIR. Dr. Collins, your full testimony will be included in the record. You are now recognized for 5 minutes for your opening statement.

Dr. COLLINS. Well, thank you, Chair DeLauro, Ranking Member Cole, and distinguished members of this subcommittee. I am honored to be here today with my colleagues representing the National Institutes of Health, the NIH.

I could spend hours describing the exciting work that the President's budget is proposing for NIH, including major investments to address impacts of the COVID-19 pandemic, reduce health disparities in maternal mortality and morbidity, improve mental health, broaden approaches to pain and opioid addiction, and establish a bold new agency within NIH called ARPA-H.

But in our brief time together it is also important to emphasize how the steady funding increases that you have provided to NIH, starting well before the pandemic, made it possible for the NIH to meet the challenges of the pandemic and to prepare for what comes next.

You know, often at these hearings I share the story of a patient whose life has been saved by NIH research. But in this uniquely challenging year, it is hard to single out any one person. In fact, all of the more than 160 million Americans who have received COVID-19 vaccines are success stories made possible by the sustained investment that this committee made years ago to basic biomedical research.

The road to these mRNA vaccines that Pfizer and Moderna now are distributing around this country and around the world actually started in the 1960s when the function of messenger RNA was first understood. These messengers carry instructions from the cell's DNA manual to produce the proteins that do the work.

For vaccines, we knew that certain proteins, like the spike proteins on this coronavirus, could spur an immune response. But might it be safer and just as effective to use RNA to instruct the patient's own body to produce these proteins?

Though it took surmounting numerous obstacles to get there, we are blown away by how well it works.

In parallel, other scientists, including some in our Vaccine Research Center, learned that locking that spike protein into the right configuration could make an even better vaccine.

So when COVID hit, we knew exactly what to do. As the seriousness of the pandemic became clear, research institutions and drug companies started off in multiple directions, competing over trial capacity, duplicating efforts, and flooding the FDA with disparate data.

NIH was prepared to step in with a coordinated playbook. Working with other agencies and industry partners, we stood up something called ACTIV, A-C-T-I-V, the Accelerating Covid-19 Therapeutic Interventions and Vaccines Partnership, and we stood it up in just 2 weeks. ACTIV's teams of public and private sector visionaries implemented objective prioritization of therapeutic candidates, knitted together clinical trial networks, and wrote master protocols to streamline approvals.

Another vital partnership NIH was able to build on was one we have with underserved communities. As we pushed to enroll pa-

tients in phase 3 vaccine trials, NIH opened a dialogue with communities disproportionately affected by COVID.

The Community Engagement Alliance, or CEAL, initiative built on existing long-term partnerships with trusted leaders in underserved communities to encourage trial participation. We were able to use the enrollment techniques we learned in large longitudinal studies, such as All of Us, that you have championed.

The result is that all Americans can look at the major vaccine trials and see that people like them were included, and CEAL has now moved on to help with vaccine hesitancy in these same communities.

Now the President's budget proposes a major investment to build on this momentum, the Advanced Research Project Agency for Health, or ARPA-H. This new agency within NIH will catalyze novel strategies to speed transformational and innovative ideas. Ideas like simple blood tests to detect free-floating DNA or protein markers that signal a cancer is growing somewhere in the body. Maybe a micro needle patch that delivers a vaccine to hard-to-reach communities in the mail. Or using an innovation funnel to recruit, test, and scale up new technologies for ambulatory blood pressure measurement with the potential to transform the management of hypertension.

Those are just three of the bold ideas that ARPA-H could tackle. But they are not science fiction. With standard approaches, they might happen in a decade or two. With ARPA-H, it could take half that time.

The President believes that, with your help, we can learn from the lessons of the pandemic and transfer this scientific momentum into big improvements in the health of all Americans. I do, too.

My colleagues and I would be pleased to answer your questions.  
[The information follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Hearing on the FY 2022 Budget Request for the National Institutes of  
Health

Witness appearing before the  
House Appropriations Subcommittee on Labor, HHS, Education, and Related Agencies

Francis S. Collins, M.D., Ph.D.

Director, National Institutes of Health

Accompanied by

Diana W. Bianchi, M.D.

Director, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

Anthony S. Fauci, M.D.

Director, National Institute of Allergy and Infectious Diseases

Gary H. Gibbons, M.D.

Director, National Heart, Lung, and Blood Institute

Norman E. Sharpless, M.D.

Director, National Cancer Institute

Nora D. Volkow, M.D.

Director, National Institute on Drug Abuse

May 25, 2021

Good morning, Chairwoman DeLauro, Ranking Member Cole, and distinguished Members of the Subcommittee. I am Francis S. Collins, M.D., Ph.D., and I have served as the Director of the National Institutes of Health (NIH) since 2009. It is an honor to appear before you today.

First, I want to thank this Subcommittee for your commitment to NIH, which allowed the biomedical research enterprise to respond quickly to the greatest public health crisis in our generation over the past year. We mounted vigorous research efforts to understand the viral biology and pathogenesis of the coronavirus disease 2019 (COVID-19), develop vaccines in record time, support and commercialize diagnostics at the point of care, and test therapeutics for both outpatient and inpatient settings. This work is far from finished.

The President's Discretionary Request proposes budget authority of \$51 billion for NIH in fiscal year (FY) 2022. The Biden Administration places great emphasis on research and development in general. At NIH in particular, the Request proposes to build on the successes of pandemic era research and to put the research enterprise to work on some of our Nation's most persistent and perplexing health challenges, including cancer, Alzheimer's disease, opioid use disorder, health disparities, maternal mortality, HIV/AIDS, gun violence, climate change, and other areas with major implications for our nation's health.

First and foremost, the President's Request proposes \$6.5 billion to establish the Advanced Research Projects Agency for Health – ARPA-H to drive transformational innovation in health research and speed application and implementation of health breakthroughs. ARPA-H will tackle bold challenges requiring large scale, cross-sector coordination, employing a non-traditional and nimble approach to high risk research, modeled after DARPA in the Department of Defense. To achieve this, ARPA-H will invest

in emergent opportunities by conducting advanced systematic horizon scans of academic and industry efforts, leveraging novel public-private partnerships, recruiting visionary program managers, and using directive approaches that provide quick funding decisions to support projects that are results-driven and time-limited. Potential areas of transformative research driven by ARPA-H include: the use of the mRNA vaccines to teach the immune system to recognize any of the 50 common genetic mutations that drive cancer; development of a universal vaccine that protects against the 10 most common infectious diseases in a single shot; development of wearable sensors to measure blood pressure accurately 24/7; and leveraging of artificial intelligence technology to advance care for individual patients and improve detection of early predictors of disease.

ARPA-H represents the kind of transformative idea for biomedical research that only comes along once in a long while. Our confidence that NIH is ready has been greatly advanced by our experience in addressing the COVID-19 pandemic – developing vaccines in record time, establishing an unprecedented public-private partnership on therapeutics that has made it possible to test more than a dozen possible therapeutics in rigorous trials, and building a venture capital model for assessing SARS-CoV-2 diagnostic technologies that has yielded millions of daily tests in just months.

But while we begin to imagine a life after COVID-19, we must acknowledge that there are COVID-related impacts that we have yet to understand and address, including the full impact of the pandemic on children. Children were largely spared from COVID-19 but for some children, exposure to the COVID-19 virus led to Multisystem Inflammatory Syndrome in Children (MIS-C), a severe and sometimes fatal inflammation of organs and tissues. The *Eunice Kennedy Shriver* National Institute of Child Health and Human

Development (NICHD) is leading a multi-institute initiative known as the Collaboration to Assess Risk and Identify loNG-term outcomes for Children with COVID (CARING for Children with COVID), which will assess both short-term and long-term effects of MIS-C and other severe illness related to COVID-19 in children, including cardiovascular and neurodevelopmental complications.

For many Americans, this pandemic and its related socioeconomic effects have had an overwhelming impact on their mental health. Prior research on disasters and epidemics has shown that in the immediate wake of a traumatic experience, large numbers of affected people report distress, including new or worsening symptoms of depression, anxiety, and insomnia. To aid in mental health recovery from the COVID-19 pandemic, NIH will continue to focus on research in this area. This will be done, in part, by utilizing participants in existing cohort studies, who will be surveyed on the effect of the pandemic and various mitigation measures on their physical and mental health.

The COVID-19 pandemic has brought into sharp focus the dramatic health disparities that exist across the American population. In addition, the Nation has been shaken by the killing of George Floyd and other attacks on people of color, forcing a recognition that our country is still suffering the consequences of centuries of racism. NIH will continue to address these disparities, specifically through research managed by the National Institute on Minority Health and Health Disparities (NIMHD), the National Heart, Lung, and Blood Institute (NHLBI), the National Institute of Nursing Research (NINR) and the Fogarty International Center (Fogarty).

NIMHD looks to better understand the human biological and behavioral mechanisms and pathways that affect disparity populations, better understand the long-term effects of



disasters on health care systems caring for populations with health disparities and research focusing on the societal-level mechanisms and pathways that influence disease risk, resilience, morbidity and mortality. NINR and Fogarty both look to better understand and reduce rural health disparities in low-income counties in the southern United States, support nursing science focused on racial, ethnic, and socioeconomic health disparities, with the goal of closing the gap in health inequities and increase health disparity research in low and middle income countries.

In addition to the core health disparities research, the President's Request puts an additional specific focus on maternal morbidity and mortality (MMM), which disproportionately affect specific racial and ethnic minority populations. Black and American Indian/Alaska Native individuals are two to four times more likely to die from pregnancy-related or pregnancy-associated causes compared to white individuals. Furthermore, Black, Hispanic and Latina Americans, Asian, Pacific Islander, and American Indian/Alaska Native individuals all have higher incidence of severe maternal morbidity (SMM) compared to white individuals. The Implementing a Maternal Health and Pregnancy Outcomes Vision for Everyone (IMPROVE) initiative supports research on how to mitigate preventable MMM, decrease SMM, and promote health equity in maternal health in the United States.

As the climate continues to change, the risks to human health will grow, exacerbating existing health threats and creating new public health challenges. Major scientific assessments document a wide range of human health outcomes associated with climate change. While all Americans will be affected by climate change, underserved populations are disproportionately vulnerable. These populations of concern include children, the elderly, outdoor workers, and those living in disadvantaged communities. NIH is poised to lead new

research efforts to investigate the impact of climate on human health, with the goal to understand all aspects of health-related climate vulnerability. Therefore, the President's Request includes a \$100 million increase for research on the human health impacts of climate change.

The FY 2022 President's Discretionary Request makes a major additional investment to address the opioid crisis. The crisis of opioid misuse, addiction, and overdose in the United States is a rapidly evolving and urgent public health emergency that has been exacerbated by the coronavirus pandemic. Since the declaration of a public health emergency for COVID, illicit fentanyl use and heroin use have increased, and overdoses in May 2020 were 42 percent higher than in May 2019.

The use of opioids together with stimulants, such as methamphetamine, is increasing; and deaths attributed to using these combinations are likewise increasing. Taking note of these trends, FY 2021 appropriation language expanded allowable use of Helping to End Addiction Long-term (HEAL) funds to include research related to stimulant misuse and addiction. Identifying how opioids and stimulants interact in combination to produce increased toxicity will enhance our ability to develop medications to prevent and treat comorbid opioid and stimulant use disorders and overdoses associated with this combination of drugs.

Finally, I'd like to take a moment to thank this Subcommittee for its recognition over the last two years that America's continuing leadership in biomedical research requires infrastructure and facilities that are conducive to cutting-edge research. With your support, we will break ground in the near future on a new Surgical, Radiological, and Laboratory Medicine division of our Clinical Center, which will replace severely outdated and deteriorating operating suites and lab space with state-of-the-art facilities. NIH

continuously works to ensure that the buildings and infrastructure on its campuses are safe and reliable, and that these real property assets evolve in support of science – but NIH’s backlog of maintenance and repair is now nearly \$2.5 billion. The President’s FY 2022 Discretionary Request includes \$250 million to make progress on reducing this backlog and requests flexibility for Institutes and Centers to fund construction, repair, and improvement projects.

COVID-19 compelled us to perform a stress test on biomedical research enterprise. The enterprise performed nobly. We found what worked, and also identified barriers we hadn’t fully appreciated before, and invented new ways around them. The President’s FY 2022 Discretionary Request is a roadmap for how to build on the successes of research, address our gaps, and apply our insights to the most important problems we face as a nation. With your support, the future is filled with opportunity. My colleagues and I look forward to answering your questions.

The CHAIR. Thank you. Thank you very much, Dr. Collins.

I just want to say, I sometimes make reference to this panel when you come up, and I use the Yankee baseball team, talking about the power and the hitting power of Murderers Row. But today I just want to talk about Healers Row and really extraordinary work that has translated to the benefit of so many and have already saved so many lives. So thank you for the work that you do.

I know that you can't share so many details about the structure of ARPA-H. That will be, I understand, in the President's budget. You just started to talk about some of the things. I have kind of three questions in this area.

Again, share some examples of the kind of research that this might support and how it differs from the types of research typically supported by the NIH.

How is ARPA-H different than NCATS, which was established a decade ago, and that was about promising medical research into treatments and cures that are available, and how is this approach different?

And then I just wanted to ask about how ALS research could benefit from the high risk, high reward accelerated approach proposed by ARPA-H.

Dr. COLLINS. Well, thank you. That is a wonderful set of questions. And I want to tell you that my colleagues and I are really excited about the potential that ARPA-H offers for us to move biomedical research even more nimbly and aggressively forward to make the kinds of discoveries that the public is waiting for.

We learned a lot in the space of our experience with COVID-19 about how it is possible when there is an urgent sense of the need for clinical advances to happen at unprecedented speed. And that happened with vaccines. That happened with diagnostics. That happened with setting up therapeutic trials. And from that, we have gathered the general sense that this momentum ought not to be lost.

In talking with all of the 27 institutes and centers, the notion of taking the DARPA approach to biomedical research has gathered a lot of enthusiasm. DARPA, as you know, as part of DOD, has had that experience of moving things in a very bold and risk-taking way. And that is why we ended up with the internet and with GPS and with self-driving cars and a long list of other things.

And we think there is a subset of biomedical research that would also be amenable to this kind of approach. This would involve program managers who are given the flexibility to identify in an area of opportunity ways that you could bring together partners who might not normally write an NIH grant—those might be academics, they might be small businesses—and figure out how to create the kind of momentum with appropriate financial support to move things forward at unprecedented speed.

You could think, for instance, taking what we have learned about messenger RNA for COVID-19, and speeding up the process of cancer vaccines, which are showing a lot of promise but could go faster.

What about something such as a new approach to hearing aid development, which has been a little stuck in one place and might

greatly be advanced by this kind of innovation funnel or “Shark Tank”?

Such things as using the technologies we now have to learn ZIP Codes of all of the human cell types so that you could deliver drugs or gene therapies in an appropriate and rapid fashion.

Those are all ideas that are coming up. Every one of the 27 institutes and centers is hitting me with lots of great ideas.

The CHAIR. So tell me how this differs from NCATS.

Dr. COLLINS. So I am very much proud of NCATS, having had a lot to do with nurturing that idea, coming up with something that would provide translational efforts, and they have in things like tissue chips, in terms of making high-throughput screening available.

But it is on a modest scale. Most of NCATS is supporting the CTSAs, a very important part of our clinical research effort.

This basically takes the NCATS model and puts it on steroids, takes the kinds of things that have been in the Cure Acceleration Network and makes it possible to do so at a much more rapid pace and across all diseases in a way that all the institutes at NIH can join in on and very much want to.

So, yeah, I think it is building on that experience, but taking it to the next level.

The CHAIR. I understand that, but just let me ask you this then. What happens with NCATS? If we are going to build on that, do we then fold in this? Do we then have one area that we are looking at here rather than two, ARPA-H and NCATS, and then we just create one effort?

Dr. COLLINS. It is a very good question, Madam Chair. I don't think we have a completely clear best option at the present time. It might be possible, for instance, for the CTSAs to move into ARPA-H or potentially to stay where they are with NCATS. We might take the Cures Acceleration Network model and move that into ARPA-H.

Those are all issues that need to be worked out. We need a lot more input now that we can talk more publicly about this, or we can in a couple of days, to get input from stakeholders.

The CHAIR. It would appear to me that when you talked about Alzheimer's, diabetes, and cancer with regard to ARPA-H, I don't know where ALS fits in that and was that left out for some reason. And it is a devastating neurological disease, as you know.

Dr. COLLINS. Yes.

The CHAIR. And there are no current effective treatments to stop or even slow the progression, as I understand it, and you know I am not a scientist.

Dr. COLLINS. So, if I may, I know the clock has run out, but just very quickly.

Cancer, Alzheimer's, and diabetes were put forward as examples of common diseases that ARPA-H could work on. But the intention is for this model to be applied to all of the diseases that are ready for this scientifically.

And I think ALS is a great example. Already had conversations with the Neurology Institute about an ARPA-H project specifically focused on ALS, recognizing that we are learning some fundamental things about what happens to the motor neurons in the spi-

nal cord that could, with a crash program, be advanced much more quickly to understand the pathogenesis and ultimately new approaches to therapy using such things as RNA approaches.

So I think it is a great example, Madam Chair, of what we could do that we currently can't quite do with this new mechanism.

The CHAIR. Thank you. And I will have questions for Dr. Fauci and Dr. Gibbons.

But with that, let me yield to the distinguished ranking member of the committee, Congressman Cole.

Mr. COLE. Thank you very much, Madam Chair. And I want to build on your line of questioning because, as I said in my opening remarks, look, I am very supportive of the President's topline proposal here.

As a matter of fact, I am pleased to have a President who set out a marker. With all due respect to the last two, this committee went well beyond what was proposed here.

And so it is nice to have a partner at the other end of Pennsylvania Avenue who sees this, the value of this investment, I think the same way the chairman and I do.

Having said that, I am wondering, I look at the \$6 billion-plus investment in ARPA-H, and as you said, Dr. Collins, we still have unresolved questions and procedures.

Would it be better to start with a more modest investment—DARPA itself is about \$3.8 billion—and plow the rest of that money into our normal research? Again, I am not arguing for a reduction in total spending. I am just arguing for we are going a little fast here before we actually have this thing worked through.

So I would love your thoughts on that, with the recognition that you work for the President of the United States, so your job is to defend his proposal.

Dr. COLLINS. Thank you for pointing that out.

Mr. COLE. May be a little bit more aggressive here, although I like the instinct that he is showing.

Dr. COLLINS. Well, thank you, Congressman Cole, and I appreciate your thoughtfulness in this regard in terms of what is the right balance here.

Let me point out, though, that ARPA-H is not intended to be a freestanding entity that is sort of over here somewhere, and then you have the 27 institutes and centers over there doing something different.

This is an engine for discovery that is going to be tapped into by every one of those 27 institutes and centers, extending their reach beyond what they could do with their current budget line. So we shouldn't think of these as competitive, but rather as synergistic.

Yeah, it is a big deal to start something up with a \$6.5 billion budget. Fortunately, this has been put forward by the President as 3-year money, which would help a lot as we are sort of ramping this up.

But I believe, based upon the experience we have had with COVID-19—and again, thank you, Congress, for providing us during this crisis with, as Chairman DeLauro said a little bit ago, over \$4 billion of additional funds to help. We had no difficulty figuring out how to invest those in vaccines, in therapeutics, and in diagnostics.

And I believe, if funds are available, there are enough ideas and enough science and enough scientists out there to do the work that we could very well utilize what has been proposed by the President.

Mr. COLE. Well, good. Well, I look forward to working with you on that. I still have some concerns, but we can resolve those in dialogue because we don't have any differences on the top line here.

Let me turn to Dr. Sharpless, if I may.

One of the more both impressive and challenging problems we have had is there have been so many wonderful proposals in the area of cancer research in recent years. And while we steadily pushed up the number of money at NIH, it seems to me we have had a hard time funding all the good proposals in front of us in terms of cancer. There seems to be a lower percentage of grants funded than in most of the other areas.

So could you sort of bring us up to date where we are in funding good science and give us your thoughts as to what else we ought to be doing to make sure that we are not leaving good ideas on the table in terms of cancer research?

Dr. SHARPLESS. Thank you, Representative Cole. It is a really important topic.

I think the good news to start off with is that, thanks to the support of this Appropriations subcommittee, we have had the ability to increase our pay lines and success rates, these metrics we follow, which had gone down to very low levels because of the dramatic increase in applications to the National Cancer Institute. So applications were up 47 percent since 2013, and that is hard to keep up with.

So I think our pay line, one metric we follow, nadired at 8 percent, but is now up to 11 percent, so that is a 35 percent increase in the last 2 years, which I think is good progress, but that is still a pretty low support rate.

I think we would like to get to a number that would be more like 15th percentile, which would match sort of the rest of the NIH a little more closely. As you know, there are a lot of important things we support outside of that pool that we have to fund as well.

So I think that this is a good problem in some ways. It says there are a lot of scientists coming to NCI with ideas that are very, very valuable, and we need to be able to get to them all. And the support of this subcommittee has been very important in the past, but I think that is still an area where our pay lines are still too low.

Mr. COLE. Well, we don't have a lot of time left, so I am not going to use all mine. But I want to say I am glad you are back at the NCI after your stint at the FDA. I know you did a great job there, but we really like you where you are at and appreciate the job that you have done.

I have got a lot of questions, like you do, Madam Chair, but I will hold them for the next round, and I yield back.

The CHAIR. I thank the chair, and I appreciate that question to Dr. Sharpless. It is a question that I had as well. So thank you very, very much. I say that to the ranking member.

Now, Congresswoman Roybal-Allard.

Ms. ROYBAL-ALLARD. Thank you, Madam Chair.

Let me begin, Dr. Collins, first of all, by joining my colleagues in thanking you for the incredible work that you do. However, I

would like to address my questions with regards to the ECHO program.

It has been 6 years since the congressionally directed National Children's Study was prematurely canceled, despite an investment of approximately \$1.5 billion over its 14 years of planning and implementation.

At the time of its termination, without informing Congress, this subcommittee was guaranteed that newly developed environmental influence on child health outcomes, quote, "would make use of the existing maternal pediatric cohorts that were recruited through the National Children's Study."

We were further reassured that the ECHO program would attempt to answer many of the original seven critical research questions about the environment's influence on child development and health.

We are now 6 years into what was designed to be a 7-year program, and it is my understanding that over 67,000 children are being followed in longitudinal core study factors affecting child health in the areas of [inaudible] Child development and well-being.

Which of the original NCS study questions are being addressed through the ECHO program? And can you give us some examples of the research that is being done utilizing these cohorts?

Dr. COLLINS. Thank you very much, Congresswoman, for the question. I am going to turn to Dr. Diana Bianchi, Director of the National Institute of Child Health and Human Development, who has been quite engaged as one of the advisers for the ECHO program, which is managed by Dr. Matthew Gillman.

Dr. Bianchi.

Dr. BIANCHI. Thank you, Dr. Collins and Representative Roybal-Allard.

As you know, the ECHO program brings together 72 different cohorts, and they are currently doing observational studies of over 50,000 children.

One of the most impactful studies that has recently been completed has looked at women entering pregnancy and looking at the connection between a healthy weight in the mother or the pregnant woman and eating a healthy diet during pregnancy, and that has resulted in a statistically significant decrease in the rate of pre-term birth.

And, interestingly, it was significant in both Black and White women, because Black women do have a higher incidence of pre-term birth. So that is quite impactful.

In addition, NICHD is working with the ECHO program on an interventional study using the IDeA States Pediatric Clinical Trials Network, which is part of the ECHO program, and we are working together to provide comparative effectiveness studies to determine how best to treat neonatal opioid withdrawal syndrome.

So these include pharmacology-free intervention, which is eat, sleep, and console the babies, as well as a weaning trial, and we have trials planned for the future to look at buprenorphine in infants.



Mrs. ROYBAL-ALLARD. Okay. I have several questions regarding this program, but I will just go to my last question because time is running short.

Is the NIH considering extending the ECHO program, given that the original NCS study was designed to follow children from birth through age 21, and the cohorts, as I understand it, have not yet reached the age of 21?

Dr. BIANCHI. Dr. Collins, do you want to answer that since the program sits in the Office of the Director?

Dr. COLLINS. Sure.

No, I think that is a very important question, and we do want to fully realize the potential of this very important cohort of over 50,000 kids. And, obviously, the time is about right in the course of the next year to figure out exactly what that future course will be.

We have engaged internally in some deeper discussions about that, and we would like to get back to you, Congresswoman, about possible paths that we might take this forward.

But I do want to endorse how critical we see the ECHO program is for answering all those questions that you and we are quite concerned about.

Mrs. ROYBAL-ALLARD. Okay. Well, I hope it will continue because, as you know, the purpose was to evaluate the effects of chronic and intermittent exposures on child health and human development in the United States. And it would actually be the first study to collect this broad range of environmental exposure measures for a national probability sample of 100,000 children followed from birth or before birth at age 21.

And this is extremely important for communities such as the one that I represent because it looks at the disparities of children in rural and underserved communities which often have greater health issues and problems. So I am hoping that you will find a way to continue this program because, as you said, it is extremely important.

I yield back the balance of my time.

The CHAIR. Congressman Harris.

Mr. HARRIS. Thank you very much.

And thank you all for being here again this year.

One of the things that we have to do is provide some oversight of the moneys that have been appropriated to NIH. For instance, this morning's front page story in The Wall Street Journal is the Wuhan lab leak debate. So this continues to be discussed. And I just would like, Dr. Collins, maybe just a couple of clarifications.

I understand we did not directly fund the Wuhan Institute of Virology, but my understanding is we did send about \$3.7 million in grants to EcoHealth Alliance, of which \$600,000 went to the Wuhan Institute of Virology to various studies there. Is that true?

Dr. COLLINS. That is correct. I am going to ask Dr. Fauci also—

Mr. HARRIS. No, I only have 5 minutes. I just need that is true, okay, because I read it. That is true.

Do we know whether the Wuhan Institute of Virology does gain of function research?

Dr. COLLINS. They were not approved by NIH for doing gain of function research. We do not—and that is the official governmental identification of that term, by the way. We are, of course, not aware of other sources of funds or other activities they might have undertaken outside of what our approved grant allowed.

Mr. HARRIS. Okay. So we could have sent money through EcoHealth Alliance. Money could have ended up in the Wuhan Institute of Virology, which might be doing gain of function research. And, in fact, since they sent a general of the Communist Party Army to take over the lab in February 2020, it is not out of the realm of possibility they are doing that.

So because I do know that money is somewhat fungible once you send money to institutes, it bothers me a little bit that we would send money to an institute that might be doing gain of function research, especially China.

Do we send any money to any sub-agencies or sub-grantees that could be sending money to Russia?

Dr. COLLINS. I don't know the specific answer to that. I think we have in the past, and I don't know whether we currently do or not.

Mr. HARRIS. Okay. And we will submit it as a QFR, if you could get back to us about that.

Now, in Nature.Com, a publication occurred in last September about the development of humanized mouse and rat models with full thickness human skin and autologous immune cells.

Dr. Fauci, this was funded out of the NIAID. It involved scalp skin transplants from 18- to 20-week aborted fetuses.

And what I want to know is, does the NIH ever follow up on how these specimens are obtained on a mid-second level—mid-second trimester aborted fetuses for studies like this?

Dr. FAUCI. Well, Dr. Harris, that grant and that study you are referring to was gone through all the appropriate guidelines and oversight. So I am not sure exactly what you are asking, but all of the research that comes out of that was done with the appropriate oversight and guidelines that have to do with fetal tissue research.

Mr. HARRIS. Okay. So I will—again, I will submit a QFR. Perhaps if you could send me what the NIH knows about how these tissues were obtained.

You know, I don't know, the idea of taking 18- to 20-week human fetus scalps, obviously, this would have to result from decapitation because you have to harvest the scalp, implanting it on the backs of rats. I am just not sure that is something we should be involved with to any significant level.

Now, one issue that has come up is the question of research on the immunology of COVID. And the immune response T cells, I think, are going to be found to be fairly important, and I think most people recognize they are pretty important in determining immune response.

Would measuring T cells and T cell immunity, especially in people who have had the disease, would that be of interest? And if so, is the NIH urging the FDA to promote the EU, emergency use authorization, for T cell testing, which is not widely available but may be very useful in informing us about the immune response?

Dr. Collins.

Dr. COLLINS. I think, yes, FDA is intensely interested in this. I don't know that we have to particularly urge them. They have approved one T cell test from adaptive technologies, and I know they are interested in looking at others. And I agree with you, this is a very important part of understanding immune response to COVID.

Mr. HARRIS. Dr. Collins, I will have to inform you that they are not, and they have, in fact, informed other companies that this is not a priority for FDA and they are not actively looking at further EUAs.

But my time is up. I yield back.

The CHAIR. Congresswoman Lee.

Ms. LEE. Thank you very much. Thank you, Madam Chair and Ranking Member.

Thank you to Dr. Collins and all of our directors for your tremendous leadership.

And thank you, Dr. Collins and all of you, for really fighting so hard to crush this virus, and all of the work that you have done, you said for the last 30 years, in just getting us prepared to save lives and to address the coronavirus. So thank you so much.

Let me ask you, Dr. Collins, we have talked a little bit about the continued commitment to address disparities of Black men and women in science and medicine. And I would like for you to share how NIH has incorporated the findings of the recommendations of the National Academies of Sciences' Roundtable on Black Men and Women in Science, Engineering, and Medicine to address really the—and it is a major, alarming underrepresentation of Black men in the medical schools and in the medical profession.

That is the first question. I am going to do a couple of questions at one time.

Also, just in terms of health disparities, Dr. Collins, let me ask you, what specifically—and I know NIH is committed to this—but specifically to address the health disparities stemming from structural racism and more research and resources into behavioral health, trauma-related informed mental healthcare, diversity in clinical trials, diversified workforce, all of the major issues that address African Americans, people of color, within the whole—within the health space, the National Institutes of Health, as it relates to dismantling structural racism and building systems which include equity and justice.

Dr. COLLINS. Well, thank you, Congresswoman Lee. I think those questions actually I can fold into a synthesized response, because we at NIH are deeply invested in taking a very fresh and aggressive look at what we can do about the problem of structural racism in the United States, which we have come to recognize is something that affects all institutions, and that includes the biomedical research institutions that we support.

And I have to recognize this is the one-year anniversary of the killing of George Floyd, which I think was a very significant event for many people who had somehow imagined that we were past the point where racism existed in this country. And we at NIH took that and other episodes like that very seriously and have formed together an effort called UNITE, U-N-I-T-E.

There are five groups in UNITE, each of which has a specific focus. One is on the workforce. And you specifically have highlighted the problem about the diminishing numbers of Black men going into medicine and medical research, and that is a concern.

But, frankly, we have a much broader set of concerns. When you look at the diversity of our workforce, it does not look like our country.

We have worked hard on that, Congresswoman, and we have made some progress, if you look at the numbers of those who are applying for grants and getting funded, but we are still well short of where we need to be.

We aim with this UNITE initiative to make a much stronger push in that direction, both in terms of recruiting and retaining. Because it is one thing to recruit Black men into medical research. It is another if they find an environment that is not welcoming, and then they don't stay. We have to work on that part as well in terms of our whole culture, our whole environment.

And then, when it comes to health disparities, we are aware of the facts that health disparities are oftentimes based upon deep-seated structural racism in our environment, in our culture. And it is not sufficient for us to categorize the various factors. We need to invest more in interventions to see how those can be changed.

We have announced a Common Fund program of \$24 million, it is already out there, to do transformative research on health disparities. And we have a joint funding announcement that now involves a whole bunch of institutes, led by the Minority Health and Health Disparities Institute, that is putting another \$30 million into research in fiscal year 2022 on this very topic.

We will be publishing in the fairly near future a broad description of this UNITE initiative that I think all of the members of the subcommittee will be interested in.

I just want to tell you, personally, of the things that happened in 2020, COVID-19, well, yeah, we will all remember that. But I think we also had this wakeup call that we have to address this issue of structural racism. And my colleagues and I are determined to do so in a bold, energetic, and determined way.

Ms. LEE. Thank you so much, Dr. Collins. And we will follow up on the specifics in terms of the budget.

Very quickly, Dr. Fauci, good to see you. HIV and AIDS. We know you recently were addressing the COVID-19 virus, but you played such an important role in HIV and AIDS early on. How far backwards have we gone now as a result of the COVID virus, and will we achieve an AIDS-free generation?

Dr. FAUCI. I don't think we have gone—thank you for that question, Congresswoman Lee. I don't think that we have gone backwards. Obviously, when you shut down a society, the accessibility for testing and for the chain of drug availability can be disrupted, the way everything is disrupted in this very terrible time, including vaccinations for children and things like that.

However, there have been a number of really important advances that have been under the radar screen with regard to HIV and AIDS. For example, the demonstration that cabotegravir, the long-acting injectable, can be very adequately used for pre-exposure pro-

phylaxis, which I think is going to increase dramatically the adherence to that.

And as I have discussed with you in the past, the PrEP, pre-exposure prophylaxis, is an important ingredient in our attempt over the 10 years from 2020 to 2030 to end the epidemic in the United States. And I believe, notwithstanding COVID-19, that we will achieve that goal as trying to implement many of the things that we are doing.

So although it appears that things have been under the radar screen, they have, in fact, been going on I believe at a good pace. But thank you for that question.

Ms. LEE. Thank you. Thank you, Dr. Fauci.

Thank you, Madam Chair.

The CHAIR. Thank you.

Congresswoman Herrera Beutler.

Ms. HERRERA BEUTLER. Thank you, Madam Chair. And like everyone else, this is probably my favorite hearing of the year, just getting a chance to talk with really the world class experts on just about everything.

I have a few different questions. The first one, Dr. Collins, I think would be for you.

Last year I requested that NIH develop a comprehensive pediatric research agenda to study the impacts of COVID-19 on children and to report to this committee in 120 days. And I wanted to ask about the status of that report, and what are the NIH's maybe preliminary findings and plans for this research agenda.

Dr. COLLINS. Well, it was a very appropriate assignment to give us, because we know that children have been affected significantly by COVID-19. They can get the illness. They can have this strange and somewhat unusual outcome of MIS-C, Multi-System Inflammatory Syndrome of Children. They also can get long COVID where they don't seem to recover. And we have a big effort on this.

Actually, if I may, I would like to call on Dr. Bianchi, our pediatrician, who can tell you a bit more about what we have been doing.

Ms. HERRERA BEUTLER. Great. And I apologize. I have a couple of questions I am going to fit in here, so—

Dr. BIANCHI. Okay. I will try to be brief.

But, as you know, almost 4 million children have had positivity for SARS-CoV-2. The critical question is, of those children, most of them are going to be mildly affected, but who is the one in a thousand who is going to get very sick with Multi-System Inflammatory Syndrome in Children, requiring perhaps an ICU stay and perhaps serious illness and death?

To address this through the RADx-rad program, which is developing radical approaches to testing, we are leading a program, a trans-NIH program called PreVAIL kids, which comprises eight different programs that are all taking a different piece of the pie and are looking at children who, for example, come into the emergency room with a fever. Do they have COVID? Are they going to be at risk for MIS-C?

And all of these different programs are taking biospecimens and using bioinformatics to predict who is going to get sick with MIS-C and then possibly the long COVID.

Ms. HERRERA BEUTLER. Do we have that preliminary information? Do we have some answers on that?

Dr. BIANCHI. No. The program has started within the last few months.

Ms. HERRERA BEUTLER. Okay. Okay. I am interested to be kept abreast of that. Thank you, Dr. Bianchi.

Dr. BIANCHI. Absolutely.

Ms. HERRERA BEUTLER. You know, I read something earlier this week about how 16-year-olds, I think it was with Moderna's shot, after 4 days show an enlarged heart. I have seen other things about different kids and how it impacts them. And I cannot stress enough how important I think it is that we turn our attention to the children as it relates to the pandemic.

One of the things I do have some challenges with—my 2-year-old just hopped on my lap, and she hopped off—the mental health and developmental issues that these kids have been through in the last year.

Like, I took my kid, my youngest, to Costco. She hadn't been in a big box store. It kind of flipped her out, seeing that many people. That is a small thing, right?

I think about telling a 2-year-old who maybe is in daycare, you have to wear a mask now all day long, and all the other kids have masks. There is learning and speech developmental issues. There is interaction.

So my 2-year-old doesn't speak very much yet. We read a ton to her. But so much of what we do is nonverbal. In fact, most communication is nonverbal anyway.

I am really concerned that now that we have reached this point where you can get a vaccination if you want one, that we are further putting the burden on children to keep the adult population safe by telling young children, "Indoors, outdoors, you are going to mask."

While everybody else is now feeling this sense of freedom, we are putting more of the burden on kids—who have, I believe, borne the disproportionate share of this, whether it is school and learning loss, mental health, possibly domestic violence, all these different things that we are not going to know for the next—we are going to know in the next 10 years.

I was hoping someone could speak to that. The mask mandate for children that age at this point, I need to be convinced that that is appropriate.

Dr. COLLINS. Thank you for that question and those observations.

I think we are all really concerned about this. People sort of shrug and say, "Well, kids are resilient." But, wait a minute, this is really an incredible, unprecedented challenge to their life experience.

The National Institute of Mental Health has recently issued that we are asking for grant applications to look specifically at the mental health consequences of COVID-19 for children.

What has it meant for them to be out of school, which is normally the place where a lot of socialization and education happens for this prolonged period.

And what about this issue of being fearful of an illness that might actually affect your families, might suddenly be blamed on you if you were the one who happened to bring the illness in?

I totally am with you here. There are a lot of unanswered questions. We are going to be studying that, I think, with some considerable intensity, and hopefully we can provide some better answers about how best to help.

Ms. HERRERA BEUTLER. Can we be kept abreast?

Dr. COLLINS. Absolutely.

Ms. HERRERA BEUTLER. Thank you, Madam Chair.

The CHAIR. Congressman Pocan.

Mr. POCAN. Thank you very much, Madam Chair. And thanks to everyone for being here. I completely agree with Representative Herrera Beutler. This is my favorite hearing of the year as well. I have tremendous respect for every single one of the witnesses here.

And thank you for all of the incredible work you do every single day for all of us. I just wish we could direct more of the Department of Defense funds to the defense that you are doing for this country and the defense that we needed to do so much in the last year, things like COVID-19.

I have lots of questions, but I do want to give you a chance, Dr. Collins. I think you were trying to pass a question to Dr. Fauci about the Wuhan lab. I heard lots of things like “could,” “might,” and “not out of the realm of possibility” is really hard evidence there. I believe there is some white whale narrative changing trying to occur. But if you wanted to have Dr. Fauci answer that briefly, because I do have a lot of questions, I would be glad to give some time out for that.

Dr. COLLINS. Dr. Fauci, please.

Dr. FAUCI. So, what is the question, Congressman Pocan, please? What specific question do you want me to answer?

Mr. POCAN. Well, I believe the question Dr. Harris was asking is did we fund COVID-19, my bad? I am paraphrasing it because we have 5 minutes. But that seems to be the new narrative that is out there that somehow, let's not worry about vaccinating people and getting the economy going. Let's figure out how to somehow say there is a different way this all started. And I am just kind of curious because I know you have had some interviews on this, but you were asked the question but not given the opportunity to answer.

Dr. FAUCI. Well, thank you, Congressman Pocan. Let me first say that I think one of the things that was perhaps was a subtext of Dr. Harris' question is, why do any research in collaboration with our Chinese colleagues? Well, the underlying reason for that is that we had a big scare with SARS-CoV-1 back in 2002, 2003, where that particular virus unquestionably went from a bat to an intermediate host to start an epidemic and a pandemic that resulted in 8,000 cases and close to 800 deaths. It would have been almost a dereliction of our duty if we didn't study this. And the only way you can study these things is you have got to go where the action is. So I often say somewhat tongue in cheek, you don't want to study bats in Fairfax County, Virginia, to find out what the animal/human interface is that might lead to a jumping of species.

So we had a modest collaboration with very respectable Chinese scientists who are world experts on coronavirus, and we did that through a sub grant from a larger grant to EcoHealth. The sub grant was about \$600,000 over a period of 5 years. So it was a modest amount. And the purpose of it was to study the animal/human interface to do surveillance and to determine if these bad viruses were even capable of transmitting infection to humans.

And the question of, well, did you do gain of function research? And, as Dr. Collins clearly articulated, there was nothing in the grant application and/or granting of the purpose of the grant and the description of the grant that would call for what is referred to as gain of function, gain of function meaning taking the virus that could infect humans and making it either more transmissible and/or pathogenic to humans. That categorically was not done. So that is the answer to that question.

Mr. POCAN. Thank you. So I have got minute and a half left, and I know there is going to be a second round. But in the minute and a half, I am very concerned about, I think, the more important issues of making sure we get more people vaccinated. Is there anything, initiatives or funding, that you might need from this committee to enhance vaccinations? Are you concerned of where we are at? Then a very specific question that I have had, if someone can ask—someone was concerned about spike proteins and the long-term consequences and their potential health effects on cold and flu season. So, if you can answer all of those, I will keep the rest of my subjects for the next round.

Dr. COLLINS. This goes to Dr. Fauci again.

Dr. FAUCI. I am sorry, Congressman Pocan, specifically, your question?

Mr. POCAN. Specifically, how are we doing on vaccinations? Is there anything else we need to get funding or initiatives to do that? And then, very specifically, a question about spike proteins, long-term consequences. I think there is a concern about potential health effects during cold and flu season. Some of the people who are reluctant right now that I am talking to, that was an issue on vaccinations.

Dr. FAUCI. Well, we are doing extremely well with vaccinations, as you well know. We have now more than 60 percent of the adult population has been vaccinated. The toxicities adverse events are remarkably low in this when you look at the denominator of the literally tens if not hundreds of millions of vaccine doses that have been given.

However, whenever you get adverse events, even though they are very, very rare, we obviously are interested in whether or not there is anything about the spike protein that would trigger something, such as an autoimmune reaction, that might give you a deleterious effect. Again, these things are extremely rare. We don't see anything that we can directly relate to the spike protein, but we are certainly looking for that. And there are immunologists who are right now looking to see if there is any connection there. But, again, to underscore, Congressman, these are really extraordinarily rare events.

Mr. POCAN. Thank you very much, Madam Chair. I will be ready for the second round.



The CHAIR. Thank you. Congressman Moolenaar.

Mr. MOOLENAAR. Thank you, Madam Chair. And I want to thank everybody for their participation today.

Dr. Collins, Dr. Fauci, I first of all want to congratulate you on Operation Warp Speed and the record timing to get this out, to get this working in America. I think it has been a tremendous success.

Because of the nature of, you know, how quickly the vaccines were developed, I know there is some percentage of the population that has hesitancy, kind of viewing it as somewhat experimental, kind of seeing how it all works out. And especially women of child-bearing age who would like to have children in the future, I know there have been some concerns about whether or not the vaccine would in any way affect them in a negative way. I wonder if you could talk to that and just mention if there is any evidence of any risk or concern to women who might be considering that in the future.

Dr. COLLINS. I think the evidence is actually quite reassuring, but let me ask Dr. Fauci to give a specific answer to your question.

Dr. FAUCI. Yes, thank you very much, Congressman, for that very important question. So, if you look at—the vaccine trials did not include pregnant women in the trials. There are now trials that are looking at vaccines specifically for effects in pregnant women and in lactating women. Those are ongoing right now.

However, if one looks at post-EUA, the number of pregnant women who elected to get vaccinated because of the clear indication that the effect of COVID-19 disease on the pregnant woman and the fetus is really something to be concerned about. So many, many women elected after the EUA to get vaccinated. There have been about 115,000 to 120,000 of these pregnancies, and there have been 5,000 to 6,000 of the births that have now been followed by the CDC and by the FDA. And as alluded to by Dr. Collins, there is no red flag signal at all that there is any concern about deleterious effects of the vaccine on pregnant women. This is really important because the one thing we do know for sure is that when pregnant women get infected with COVID-19, they can have a serious deleterious outcome.

Mr. MOOLENAAR. Thank you for that. And I just, I think that that message is really important to get that out there, and I appreciate hearing that directly from you.

I wanted to talk a little bit about the patent protection. And, you know, Dr. Collins, maybe you can answer this question. There has been some discussion, and I believe the Biden administration recently announced it will support waiving intellectual property protections for COVID-19 vaccines. I think everyone wants to see these vaccines readily available and the supply. But I am concerned about waiving the patent rights for these biopharmaceutical companies and how that might impact their willingness and their ability to partner with the Federal Government in the future when addressing pandemics because we are taking away significant protections for their investment in research.

Dr. COLLINS. So it is a very important question, and it is a complicated issue that no one should just assume can be superficially understood. I think all of us, companies, government, and academics, just citizens of the world believe we need to do everything

we can to get vaccinations made available to all the people who need them, and especially so in low- and middle-income countries, where the need is great and the availability in terms of the supply is low.

But it should not be assumed that it would be possible just by a quick effort over the course of a couple of months to establish vaccine manufacturing capacity in lots of other parts of the world that don't have it. These are very complicated biochemical processes, biotechnology processes that require—if you start from basically no previous experience, more than just a few months, more like years.

And so, while this, I think, is in the long term, what we need to see is this expansion of manufacturing capability, in the short term, we are going to depend on the companies that have that capacity to do as much as they can to expand their capabilities. And, certainly, I think all of us would agree that is what we need to see happen.

So it is going to have to play out over the course of time to see whether this opening up of intellectual property can help with low- and middle-income countries. But we should not assume that, in the short run, that this is going to be an immediate solution.

Mr. MOOLENAAR. Are you concerned about the long-term impact, though, and the message that sends to, you know, private sector investment and research?

Dr. COLLINS. I don't think industry is terribly concerned about that. Stephane Bancel, the CEO of Moderna, said he didn't lose a minute of sleep the night after this announcement was made by the White House. Moderna had already announced they were going to make their intellectual property available to manufacturing capabilities in low-income countries.

What is really more necessary than just the IP is the technology transfer capabilities, the skills that have to be transferred, the training that has to be done. And that is where we are going to need industry to participate, and I think they are ready and willing to do so.

Mr. MOOLENAAR. Okay. Thank you very much.

And I yield back, Madam Chair.

The CHAIR. Thank you.

Congresswoman Clark.

Ms. CLARK. Thank you so much, Madam Chair. And I share the enthusiasm over having this incredible group of panelists here today. And we have all witnessed the incredible benefits of R&D investments at the NIH, which have produced lifesaving vaccines during this pandemic. And I am encouraged by the President's vow to end cancer through proposals like ARPA-H, but I have heard some concerns that a new agency may diminish your base funding.

I know that we are eagerly awaiting the President's budget this week, but, Dr. Collins, can you do anything to assure us that this new agency can maximize its effectiveness without supplanting any funding from existing budgets at NIH?

Dr. COLLINS. I would very much like to reassure you about that. And, again, there will be more details available in a couple of days. The proposal, though, is for ARPA-H to provide an opportunity for all of the institutes to be able to take on this DARPA-like approach

to the projects that could move much more swiftly with the kind of flexibility and nimbleness and risk-taking that ARPA-H will provide. So it augments the capabilities of the rest of what NIH is about. It is not detracting from the base; it is adding a layer of translation of clinical application that can now go faster.

I would also say the way the President's budget rolls out, it proposes a \$2,500,000,000 increase for all of the rest of NIH, which is a pretty reasonable number as well. So when you put that together, I think for cancer, diabetes, heart disease, and everything else, including ALS, Chair DeLauro, we are going to have an opportunity, through all of these mechanisms, to do more. And the proposal of this total of an increment of \$9,000,000,000 is going to open up all kind of vistas of opportunity.

Ms. CLARK. Thank you. And to Dr. Sharpless, we have also heard reports that grant funding has gone down [inaudible].

Dr. SHARPLESS. Uh-oh. I think I lost Representative Clark.

The CHAIR. Let's try to find out if we can get Congressman Clark. Can anybody tell me anything? Well, maybe what we will do is to—we will come back to Congresswoman Clark.

Congressman Cline.

Mr. CLINE. Thank you, Madam Chair, and I want to thank our witnesses for being here and for their diligent work in developing the vaccine for COVID and for working with its distribution.

I want to first start by quoting from a 2011 opinion piece that Dr. Fauci and Dr. Collins wrote for The Washington Post, "A flu virus risk worth taking," where it includes that—you conclude: Along with support for this research comes a responsibility to ensure that the information is used for good. Safeguarding against the potential accidental release or deliberate misuse of laboratory pathogens is imperative. The engineered virus developed in the ferret experiments—in your column—are maintained in high-security laboratories. The scientists, journal editors, and funding agencies involved are working together to ensure that access to specific information that could be used to create dangerous pathogens is limited to those with an established and legitimate need to know.

So, when I am looking at a letter that Congressman Mike Gallagher sent to you back in early May, it says that funding for the—sorry, let me find this here—that funding was about \$17,000,000 was directed to EcoHealth Alliance, and rather than \$600,000, much of that was sent to the Wuhan lab.

Can you account for the \$17,000,000 that was allocated to Eco lab, and speak to the disparity and the amounts that you are discussing, Dr. Fauci.

Dr. FAUCI. Yeah, Congressman Cline, it is absolutely correct that about \$600,000, about \$800,000 was allocated, and about \$600,000 was spent over a 5-year period, no more than that. That comes through between \$125,000 and \$150,000 per year that went to collaboration with Wuhan. So the number of hundreds of thousands, as opposed to millions, is correct. The millions number is incorrect. EcoHealth had several millions. I don't know the exact amount that went to EcoHealth, but would be happy to get you that precise number.

Mr. CLINE. I see it now: 13.7 that was allocated to EcoHealth; 17 projects sponsored by NIAID, providing over \$7,900,000 in Federal

rewards for the research of viral emergence from bats in Southeast Asia. EcoHealth Alliance passed some of its funding to WIV, the Wuhan lab. And in 2020, NIH made efforts to obtain information from EcoHealth Alliance about Wuhan lab related to concerns about the origins of COVID-19.

It says that in your letter to EcoHealth: It is our understanding that one of the sub recipients is Wuhan lab. It is our understanding that WIV studies the interaction of coronavirus in bats. And there are now allegations that the current crisis was precipitated by the release of—from WIV of the coronavirus responsible for COVID-19. Given these concerns, we are pursuing suspension of WIV from participation in Federal programs. It is in the public interest that the NIH ensure that a subrecipient has taken all appropriate precautions to prevent the release of pathogens that it is studying.

Would you say it has come to your conclusion that the Wuhan lab was not engaged in a safe—ensuring the safety of its facility, as you wrote back in 2011? Is that your conclusion?

Dr. FAUCI. I didn't—I am sorry, Congressman Cline. I am not sure what you are reading from. I didn't write anything in, I don't believe, in 2011. You are reading from something that I don't have in front of me. Was that something that I signed?

Mr. CLINE. This is an April 2020 NIH letter to EcoHealth Alliance.

Dr. FAUCI. I think that was from Building One perhaps, but that is not from me.

Mr. CLINE. Okay. Let me just go ahead and ask real quick, have you responded to the letter to Congressman Gallagher, dated May 25, Dr. Collins?

Dr. COLLINS. There is a draft of that letter that is in the process of going through appropriate clearance and should be received by Congressman Gallagher fairly soon.

Mr. CLINE. Have you responded to the letter from House Commerce Ranking Committee Member Cathy McMorris Rodgers? She has written two, one dated March 18, one dated May 6. Have you responded to either of those?

Dr. COLLINS. Again, those responses are in the works. Those were very detailed with some 29 questions of 11 pages and 40 footnotes. So it is taking us a little while.

Mr. CLINE. All right. And you have a May 20th letter from several Senators that is waiting for an answer as well?

Dr. COLLINS. We do indeed on similar topics from Senator Johnson and others, and that is also in the works.

Mr. CLINE. All right. Thank you.

The CHAIR. Let me ask, is Congresswoman Clark back on yet? Okay.

Congresswoman Frankel.

Ms. FRANKEL. Good morning. Thank you, Madam Chair.

And thank you to the panel for your great work, for saving so many lives.

I am going to start with two questions, somewhat personal. I am the grandmother of a newborn nursing grandson. I would like to know where we are in terms of implementing any findings that will include pregnant and lactating women in clinical trials?

Dr. COLLINS. Dr. Bianchi.

Dr. BIANCHI. Thank you, Congresswoman Frankel, and congratulations on the birth of your grandson.

As you know, one of the goals of the PRGLAC Task Force was to create recommendations and then create a plan as to how to implement them. And we have already shown a big effect in our institute's priorities because we have established a maternal and pediatric precision therapeutics hub that is going to take the recommendations to the next level and create a center for knowledge around medications that lactating women can take safely and what are the effects on the newborn. So that is coming up. But also the PRGLAC recommendations influence our institute's strategic Plan, where we have a whole team dedicated to safe therapeutics and devices for pregnant women, lactating women, children, and people with disabilities.

Ms. FRANKEL. Thank you very much. If you can keep us posted on that.

Dr. BIANCHI. Absolutely.

Ms. FRANKEL. Then, of course, I have another personal question because I had a really lousy night's sleep like a lot of Americans. And, you know, I read—I have read many times that a lack of sleep is related to all kinds of health problems, cognitive impairment. And I am just curious—and that most Americans are not getting the recommended amount to sleep. I am just curious, what kind of research is being done in order to help us sleep better?

Dr. COLLINS. It is a great question, Congresswoman. As one of those who is not getting enough sleep, I resonate with your question very personally. And I bet a lot of the other people I am looking at on this screen are in the same boat trying to wrestle with all of our responsibilities, especially with COVID-19.

Yeah, we have a whole program on sleep research. It is part of the National Heart, Lung, and Blood Institutes. And Dr. Gibbons, as the director of that institute, might want to take a quick shot at your question about sleep research.

Dr. GIBBONS. Sure.

Thank you, Congresswoman Frankel. And as you say, it is a common challenge we all face, but it is clear that sleep and its restorative power are really important to our functionality. And, indeed, disturbances of sleep appear to affect almost every organ in the body. The body has its own natural rhythm. It affects your blood pressure, and your body's temperature. In fact, every cell in your body has a clock that has a rhythm that aligns with the clock. And when it is perturbed, it can promote diseases; a number of them related to obesity, diabetes, heart disease. When you have a heart attack, it is all influenced by sleep and circadian rhythms.

In fact, one of the studies we have been doing in collaboration with NIH's child health institute relates to, again, women in pregnancy. And what we have learned is that many women develop a sleep disturbance during pregnancy. That is surprising to men, well-known by women. And, indeed, those sleep disturbances in which you stop breathing can impair and have an influence on the course of the pregnancy and on the child. In fact, we are doing an intervention study after making that observation to see whether interventions that reduce sleep apnea, which is stopped breathing

during sleep, can actually improve outcomes of both mom and child.

Ms. FRANKEL. Dr. Gibbons, sorry to interrupt, but now you are really getting me nervous about this. But what is the cure for us that are—for people who are not sleeping? What are you suggesting, or what are you researching?

Dr. GIBBONS. There are simple things that you can do. As it turns out, a lot of them are probably what your grandmother told you is, when you get good exercise, you tend to have a better sleep. When you have a healthy diet and when you watch your screen time, particularly at night, and when you avoid all those distracting noises or eating late and you actually rest and start to cool down before you go to sleep, all those sleep hygiene habits are non-pharmacologic and can help you get a better sleep.

Ms. HERRERA BEUTLER. So, basically, we are all toast. Like none of that is going to happen. We are all toast. Excuse my language.

Ms. FRANKEL. I just want to know if there is a pill.

Dr. GIBBONS. Well, our hope, is that, in fact, lifestyle and even nonpharmacologic things as well as medication can help. Certainly, in the disease context, we are looking at sleep medications that can be nonaddictive. A key part of it is in the NIH common fund where we are looking at, how can we figure out biomarkers of sleepiness as well as understand the restorative, refreshing parts of sleep in ways that might be manipulated therapeutically?

Ms. FRANKEL. Thank you. I am going to follow up with you.

And I will share the research, folks.

I yield back.

The CHAIR. Thank you very much, Lois, for opening up the Pandora's box here for all of us here.

I understand that Congresswoman Clark is back on. So let me yield to Congresswoman Clark.

Ms. CLARK. Well, thank you, Madam Chair. I hope this is a more successful outing.

I had a brief question for Dr. Sharpless about NCI. I just wanted see if he can review for us why the National Cancer Institute needs more funding while we are seeing a decline in grants being awarded at the same time?

Dr. SHARPLESS. Sure. So, Congresswoman Clark, our grant applications are up 47 percent. So we have got this massive influx of new ideas to the NCI. What has gone down is our ability to fund a large percentage of them because with that many coming in, it is hard to—the pay lines and success rates are on the decline.

So, you know, they nadired at about 8 percent 2 years ago, which the success rates are a little higher than that. But that is an important metric. They have now come up to 11 percent, which is progress, but it is still too low. You know, this is one of the things that is keeping me up at night, frankly, is the idea that there is this great investigator-initiated science and these pools of grants that we are not able to get to. So, for example, that pool of money has funded things like checkpoint inhibitors to cure melanoma, the CAR-T cells to cure the leukemia and drugs, problems like that, and then, you know, things like PROTACs, this new invention to do medicinal chemistry that is all the rage in the pharmaceutical industry presently. All of this came out of this pool of moneys. So

it really drives progress in cancer research. And if 89 percent of them are not getting funded, that makes me very anxious.

So I think that that is our problem is that we need further support to reach these great ideas because there may be a cure for pancreatic cancer in there. And that is why we really need to support them.

Ms. CLARK. Well, thank you. Thank you for that explanation. And Doctors Volkow and Fauci, I want to talk a little bit about COVID survivors who have long-term symptoms. It has come to my attention that patients that have different symptoms, fatigue, depression, brain fog, also can have significant muscle and bone pain. And we are seeing [inaudible].

The CHAIR. We will get back for a final question.

Congresswoman Bustos.

Mrs. BUSTOS Thank you, Madam Chair.

And, obviously, if Katherine comes back on, I am happy to either yield time to her or—

The CHAIR. Sure.

Mrs. BUSTOS [continuing]. I can start all over as well.

Dr. Fauci, I would like to talk to you a little bit about vaccine hesitancy. We have seen the polls out there, the research out there that talks about the top reasons why people aren't taking the vaccine. They want more evidence that it is safe. They don't think COVID will seriously impact them. They already had COVID and have antibodies. I think those are the top three reasons that we are hearing about. This is more prevalent in rural America, much like the congressional district that I serve, very, very rural.

I saw also a poll that found that it is 21 percent of rural residents are saying now that they definitely would not get a vaccine as compared with about 10 percent of those who live in more of our bigger cities.

So what we are seeing on the ground here in the State of Illinois, we have 102 counties altogether. So we have got of the 15 least populated counties, 8 of them are overall the least vaccinated counties. And then, of the most populated counties, we have got 11 of those 15 that are doing the best. So, again, we are seeing this divide on the ground. We are certainly seeing it in the district that I serve.

I am wondering, Dr. Fauci, as a trusted voice in all of this, what do you have to say to the folks who are holding off getting vaccinated for the reasons that I just listed?

Dr. FAUCI. Well, thank you for that question, Congresswoman Bustos. The answer is the first thing we have got to do is make sure we don't point fingers at them to do that and make them feel guilty about that. But you try to explain to them each and every one of the potential reasons why they feel they don't want to get vaccinated. One of the most common is that "this was done so quickly that I am not sure that it is safe. And that you have got to get trusted messengers out there to interact with them. And when I say "trusted messengers," what we put together is a COVID-19 community corps where there have been thousands of trusted messengers. They could be sports figures, celebrities in the entertainment business, clergymen, we find and women, we find are having an important role in getting out and extending them-

selves to address each and every one of the reasons because if you just take the time to examine those reasons, there is a really logical firm scientifically sound counter to each of those concerns, including the safety, including the quickness that it was done, et cetera.

The other thing that we have found interesting that if you make the capability of getting vaccines to the hesitant people as easy as you possibly can, that mitigates some of the concern. For example, right now, in 40,000 pharmacies, including pharmacies that are located in areas that are the rural areas that you are talking about, that anyone can get to a pharmacy within 5 miles of where they are no matter where they live, that you can go now, walk into a pharmacy, you don't need a computer, you don't need an appointment, you don't need anything, you just go in and get vaccinated. The same things for mobile units to going into the rural areas when people don't have the transportation capability to get to a place. So there are a lot of things that we are doing.

Obviously, we are concerned about vaccine hesitancy because we want to get as many people vaccinated as quickly as we possibly can. But there are many things going on now to try to address that, particularly in those areas that you correctly indicated are more likely to not want to get vaccinated.

Mrs. BUSTOS. Dr. Fauci, in addition to—I am thinking of, we have got one county in this congressional district that I represent, which is pretty much the entire northwestern corner of the State of Illinois, we have one county where the entire population of the county is a little more than 6,000 people. The vaccination as of this morning—I get a daily report on this—is 19 percent. And so I appreciate—here was part of the problem too. They have one phone line to sign up to get the vaccine. That grown now to two. The high-speed internet is a problem in a very, very rural county; this is along the Mississippi River. Is there—I don't know. I am just trying to—I want to do everything that I can to help get those numbers up. But you have got pharmacies. You have got validators. Anything else when you think about a very rural part of the country that we might be able to help as Members of Congress, or any other ideas you have in a county like I just spelled out.

Dr. FAUCI. Yeah, I think mobile units would likely be one of the most important things to do because you are describing people who don't have real ready access to the kinds of things that would make it really easy.

Let me get back to the medical unit at the White House and see if there is anything that could be done. Because I believe mobile units to bring the vaccines to those rural areas are probably the best way to do that.

Mrs. BUSTOS. Okay. All right. Well, we would welcome any of that. I am out of time. I am sorry. But I can't ask my second question that I was going to ask Dr. Collins about Down syndrome. Maybe we will revisit that another time.

Thank you very much, Dr. Fauci.

And, again, Dr. Collins, to you and your entire time, thank you for all you are doing to help people.

With that, Madam Chair, I yield back.



The CHAIR. We will have a second round, Congresswoman Bustos. So, if you can stay, you know, I would be happy to get your question on Down syndrome.

I am going to ask again if Congresswoman Clark is—

Ms. CLARK. I am here. Can you hear me?

The CHAIR. Yes, go for the last bit here with your second—and then we are going to have another round, Katherine.

Ms. CLARK. Okay. Super quick, I am concerned about the rise in prescriptions for COVID long-haulers to address some of the bone pain and other medical pain they are experiencing. I wonder if this concern is shared by Dr. Fauci and Dr. Volkow, and if we are looking at nonopioid treatments for the neurological effects.

Dr. COLLINS. Dr. Volkow.

Dr. VOLKOW. Opioids are quite addictive, and this highlights actually why it is so important that we continue training on the proper use of opioid medications but also on the proper management of pain many instances not requiring opioids, which of course triggered that whole opioid crisis. But this is also why one of the priorities of the HEAL Initiative for which we got specific funds by Congress allocated to address the challenges of the opioid crisis. One of the main initiatives is to accelerate the development of effective pain medications that are nonaddictive.

Ms. CLARK. Thank you. And thank you for your patience, Madam Chair.

The CHAIR. Thank you.

Congresswoman Watson Coleman.

Mrs. WATSON COLEMAN. Thank you, Madam Chair.

And thank you Dr. Collins and to all of your colleagues, this has been so helpful, and it is so good to talk to you scientists about the value of science.

Dr. Fauci, I have a quick question for you. I am like Lois; I have got a personal issue here. I have got an 8-year-old granddaughter that I don't want to go back to school until she is vaccinated. How close are we to getting children vaccinated from that age?

Dr. FAUCI. Yeah, you know, unfortunately, Congresswoman, I don't believe that they are going to be able to be vaccinated by the time the fall term comes. We certainly will get high school adolescent individuals vaccinated then. But the age de-escalation studies that we are doing to get to an 8-year-old would likely not be available towards the end of this calendar year, but at the latest the first quarter of 2022. I would imagine late fall, early winter.

Mrs. WATSON COLEMAN. So does that concern you about sending your granddaughter back to school under those conditions? Should we be seeking virtual, continue virtual educating?

Dr. FAUCI. Well, what the CDC and other organizations, but certainly the CDC is trying to do is, given the number of and the percentage of teachers that will be vaccinated that are already vaccinated, that there should be no reason not to get children of any age back to in-person school by the time we get to the fall term. I myself would likely, would not be—I don't have children that young, but I would not be concerned when we get to the fall.

The reason I say that, Congresswoman, because if you look at the rate of vaccinations now, what is an important factor in the safety of the children is the degree of infection that is ongoing in the com-

munity. And if you look at the last few weeks, the number of infections per day have gone down in a very steady encouraging manner, from 60,000 a day to 50 to 40 to now we are well into lower than 30.

If we get to the President's goal of getting 70 percent of adults vaccinated with at least one dose by July 4, I believe by the time we get to the fall, that even though young children might not be vaccinated, it will be really rather safe in school. I do believe that.

Mrs. WATSON COLEMAN. I pray so. I pray so. And I thank you for being such a stand-up person throughout all of this.

Dr. Collins, I am very interested in NIH as it relates to all of the space that it could improve in terms of diversity, whether it is the researchers, the clinical participants, whether it is the individuals or the groups of or the work groups that review these grants. I am interested in all of that. And in last year's funding bill, I added the language that I would ask the NIH to develop a strategic plan and establish the working group to address the lack of diversity among researchers and staff and among those who are reviewing the grants. And I realize that you had initiated the UNITE Program since March. But I really would like to know some of the specific strategies that you all are employing to get at and overcome these barriers. And I would like to know what have you been actually focusing on in these initiatives, and what is your intention with regard to continued reporting back to us on the progress which is made? I am really interested in some of the strategies that you are employing to this extent.

Dr. COLLINS. Congresswoman, those are great questions, and we appreciate your asking us for the strategic plan. I appreciate Congress also giving us a little bit more time because we are in the midst of this groundbreaking UNITE initiative, which touches on all the areas you have just mentioned.

Time is short, but I will give you one example of how we are seeking to really improve the diversity of our workforce. Most of our workforce, of course, is out there in our grantee institutions; 85 percent of our money goes to those academic institutions where the science gets done. And yet their workforce is not as diverse as it could be. And when they go to try to recruit individuals of diverse backgrounds, oftentimes they are not successful. If they are successful, individuals are recruited, but they are not retained.

A new model where we would encourage them, and this is now possible to do with an additional common-fund program to recruit not just single individuals from underrepresented groups but a cohort, and to bring them on board collectively together. Something that we have piloted in our intramural program with considerable success. And then they are not like the only person of color in their community of researchers. They have this kind of opportunity to arrive together to be mentored, to be encouraged. This is a program called FIRST, F-I-R-S-T. And I think we are going to watch closely to see what this does in terms of the expanding the capabilities of our workforce to be more diverse. And this is not just something we are doing because it is a nice idea. We know that diversity equals productivity, and we want to be sure we are not missing out on that productivity by the lack of our diversity in many of our institutions. We are going to work really hard on that.

Mrs. WATSON COLEMAN. And I thank you. I am going to want to hear about the use of HBCUs in this. And I am also going to want to understand the sort of contractual relationship you have with the grantees that are expected to bring on this diversity and whether or not their mechanism success is connected to the stability of these diverse researchers and professionals. So those are some of the areas I am very interested in.

I have run out of time unfortunately, but I yield back, and I thank you very much.

Dr. COLLINS. Thank you.

The CHAIR. Thank you.

Congressman Harder.

Mr. HARDER. Thank you so much, Chair DeLauro, for hosting this.

And thank you so much to all of our witnesses for taking the time to be here and sharing their testimonies.

I want to take this in a little bit of a different direction than what we have been doing so far and talk about asthma and air quality, which are two interconnected issues in our district. Many of the cities in the California Central Valley are classified as the most polluted cities in the U.S. for both particulate matter and ozone pollution that have a lot of the direct impacts on the health of folks in our communities, especially for kids. One in six children in the San Joaquin Valley have asthma, the highest in the State, and I believe among the highest in the country. And asthma prevalence across the valley has reached as high as 20 percent in school-aged kids.

I had childhood asthma as a kid. My brother had it. It is incredibly and heartbreakingly common in our area. We, of course, have seen that in the health data even afterwards. We have among the highest emergency room visits for asthma in California. And add in the devastating wildfires in California, as well as the respiratory impacts of COVID-19, and it really creates a lot of impact for our healthcare system, and some of the costs are high. And yet it seems like we haven't necessarily made major breakthroughs in asthma research in recent decades. And many Americans are resistant to current asthma therapies.

Dr. Gibbons, I would love to hear from you as the director of the National Heart, Lung, and Blood Institute, what can you tell us about the use of Federal funds to research and develop programming to address childhood asthma? And is there more that this committee can be doing to assist in this program?

Dr. GIBBONS. Thank you for that important question, Congressman Harder. As you point out, asthma is one of the leading chronic conditions of children, in general. It certainly affects certain communities disproportionately. You recognize the rural health challenges. In addition, we are seeing similar patterns in communities of color, inner city, underserved communities where, again, these exposures can be concentrated. Indeed, that is an area of research in part related to the ECHO Program. It is a children's study where we have been assessing that.

We have learned through those studies that exposure to air pollution, particularly early in life, actually, has influence on lung development. We have learned that lung development actually con-

tinues all through childhood, even into early adulthood. It is driving the overall reserve and structure of the lungs over time. And that is why it is so important, as you indicate, to mitigate those exposures that are happening both in these rural communities and some of the inner city communities that also occur in these hot spots or pockets of high air pollution.

We also are making progress in further defining the mechanisms of the disease, to advance therapeutics beyond the drugs that currently exist and have been used for the last decade or so. Indeed, we have been engaged in a program called TOPMed in precision medicine in which we have gathered together cohorts of children and adults with asthma in a large sequencing study to identify new mediators of asthma as a part or means of developing new targets and new therapeutics.

Similarly, we have developed a platform in which we are starting to engage in precision medicine for asthma. We call it PrecISE, where we are recognizing asthma as kind of a catch-all and recognizing that there are certain subsets of patients that may respond to particular interventions that have a certain biological impact.

Mr. HARDER. That research, I am sure—I want to make sure I have a chance to ask a second question as well. I appreciate that.

I think that is great segue to my question for Dr. Collins, which is: In the President's budget, there is proposed \$110 million for the Climate Change and Human Health Program. Can you describe some of the research projects that you expect to come from that, especially any projects that focus on health outcomes related in poor air quality and how it impacts underserved communities like ours? Do you have a big piece of where this might then go or not?

Dr. COLLINS. Absolutely. And it does tie in very nicely to the question you just posed to Dr. Gibbons. Climate change affects human health in numerous ways. People tend to think about it as perhaps it is more in the area of infectious disease. And there is a lot to be concerned about there as well as climate makes different opportunities for different pathogens to find their way into the human population.

But it also affects, as you have just pointed out, air quality, the issues that are going to relate to such things as asthma, as well as heart disease, as well as cancer. All of those are wrapped up in what we think is now an appropriate moment for an enhanced and expanded effort to understand the health consequences of climate change.

Our National Institute of Environmental Health Sciences, NIEHS, will be taking the lead on this. But already they have reached out to numerous other institutes at NIH so that we can come forward with a really exciting, very broad holistic approach to how we could tackle this issue of environmental science related to health and the effects of the climate. So I am glad you highlighted it. We are excited about the opportunity here.

Mr. HARDER. Thank you. Thank you, Dr. Collins.

I yield back, Madam Chair.

The CHAIR. Congresswoman Lawrence.

Mrs. LAWRENCE. Good morning. Thank you, Chairman DeLauro. I represent a majority-minority district in Michigan, and the past year has exposed the alarming disparities for communities of color.

I believe it is absolutely critical that we act on these disparities to develop a plan for research.

Dr. Collins, it was heartbreaking when I saw the disproportionate number of African Americans being hospitalized and dying from this past pandemic. And it is almost as if in unison the response was, well, it is expected because they have underlying conditions.

When are we going to start planning? And what is the plan to address these underlying conditions in the Black community, which I know are multiple? We have—access to healthcare is an issue, food deserts, lack of proper nutrition, obesity. We were the highest in heart disease, in cancer. And so I want us as a country to move from “Yes, this is the problem” to “This is what we are going to do.” So can you please talk to me how the Minority Health and Health Disparities Institute, when will we start see a plan and results of that?

Dr. COLLINS. Well, your question is incredibly well-articulated. And it certainly resonates with myself and my colleagues, as we really have to look at what has happened with COVID-19 as another example of just how devastating health disparities are in the United States and that those same populations that have suffered from disparities, like obesity, diabetes, hypertension, got hit extremely harder by COVID-19. And nobody can look at that and not say, “We have got a serious issue here.”

If your ZIP Code is a stronger predictor of your longevity than your DNA code—and it certainly is—there is something serious awry here in terms of the way in which structural racism, which undergirds so much of what is happening institutionally and across the country, has played out in terms of health effects.

We at NIH have been studying minority health and health disparities intensively over the course of many years. I think we are energized by these observations and again by this UNITE initiative that I have mentioned already to go deeper, to really understand not just what are the causes of health disparities—some people have cynically called that admiring the problem—but actually to intervene and to come up with studies that would involve those kind of interventions to see if they work.

We can’t fix the healthcare system in the United States. As the NIH, we are a research organization, but we can understand studies to see what would happen if you changed certain approaches to health and other aspects that are contributing to this. And we aim to do that with a new common fund program that is more progressive than what has been possible before. So we are right with you.

Mrs. LAWRENCE. Thank you, and I am on executive board of Black Caucus, and I am also co-chair of Women’s Caucus. And so my philosophy in life is that you can’t tell me what the problem is more than once because once you can identify it, then let’s get about fixing it.

My next question is about mental health. The other thing that COVID ripped the scab off during this pandemic is the critical need for mental healthcare and especially in our children.

Dr. Collins, realizing the alarming rates of mental illness, how will the National Institute of Mental Health leverage the partnerships to ensure that the grant recipients receive the cutting-edge

discoveries in this field, and how do we move mental health to the top of the—to the front of the line?

Dr. COLLINS. Well, you are quite right that this is another crisis, and COVID-19 has accentuated it. We can see that both the disease itself, which is capable of inspiring various mental health issues to depression and sometimes even frank psychosis, which is frankly the whole experience that our country has had where mental health services have oftentimes been injured by a lack of access because of the concerns about being in the physical space together.

But one bright light in all of this, Congresswoman, is the way in which, because of COVID, we have seen telemedicine finding its way into the mental health arena in ways that it previously hadn't. And we have a number of research studies underway right now that are looking pretty promising in terms of showing that that actually works really well. If there is a silver lining here, it might be that we learn how to use mental health services remotely by telemedicine in a way that benefits people who otherwise just don't have access to those services. That is just one example.

There are many other things that we need to do. We have big programs now trying to come up with new approaches to treat depression, for instance, in ways that would not be the traditional methods with the traditional drugs but other approaches that might be more successful. It is a huge broad portfolio in that particular part of NIH that I would love to tell you more about if we had more time.

Mrs. LAWRENCE. Thank you, Doctor.

Thank you all.

The CHAIR. Thank you.

What I would like to do now is I think we can move to a second round. And we will make it a 3-minute round so that—and try to please hold to the 3 minutes so we give everyone a chance to ask additional questions of our panelists.

And, with that, let me let me start off. Dr. Fauci, this was about universal flu. I am going to ask three—I have got two questions. And I want to get Dr. Gibbons in as well. With regard to the universal flu, does the mRNA technology show the promise for use in vaccines for other diseases, such as flu? Is there a hope that mRNA technology could be used to develop a universal flu vaccine? What other progress has been made in the past unit towards developing a universal flu vaccine?

Dr. FAUCI. Thank you for those important questions, Madam Chair. The answer to your first question is that the mRNA technology, which as you know is spectacularly successful in developing a COVID-19, is now being used in a number of other attempts of vaccines, including a universal influenza vaccine, including vaccines against HIV, and including in cancer immunotherapy. So mRNA is now very exciting.

It is very interesting that you asked that question about where we are with other areas of universal flu vaccine. Just today, just today, we started a phase 1 trial on the nanoparticle, using a mosaic where we have multiple different hemagglutinins—these are the different colors—that are now very, very promising because we have at least four or five different hemagglutinins to cover the waterfront of the troublesome influenza components that we are deal-

ing with. And, literally, it just started today, a phase 1 trial of simply what is called a nanoparticle mosaic approach towards universal flu vaccine. So thank you for asking that question. This is what it looks like.

The CHAIR. This is fabulous. It looks like something I would have in my office as well, Dr. Fauci. So thank you. Thank you.

Dr. Gibbons, this is about cardiovascular disease in women. In 2017, 300,000 women died as a result of heart disease. And heart disease and stroke is the leading cause of death of women in the United States. Critical, research in heart disease. Quick update, NHLBI-supported research and yeah—let me go there, and I don't think that there is—we need to have more information out about women and heart disease and what we are doing on that research. Dr. Gibbons.

Dr. GIBBONS. Yeah, thank you for that. Yes, we need to continue to beat the drum of awareness and ensure that all women recognize that it is the number one killer. We have actually—polls and surveys suggesting that we may even be moving backwards in that regard, particularly in communities of color.

The CHAIR. How much time and money are we spending on heart research for women.

Dr. GIBBONS. Well, we can give you that exact number. But is certainly one of our highest priorities. A couple of examples include leveraging the Women's Health Initiative, where we found out about physical activity in elderly women. And we are now doing an intervention study to demonstrate that it is both safe to engage in that exercise and indeed still improve cardiovascular health in elderly women.

The CHAIR. Dr. Gibbons, what I am going to do is ask because my time is out. I would like to follow up with you and get information, chapter and verse, about what we are doing on heart disease in women, and how much research, how many research dollars are being appropriated to do that? And so thank you.

And, with that, Congressman Cole, let me yield to you.

Mr. COLE. Delighted. Thank you. As the chair, you are never out of time, number one. Number two, when you held the—when Dr. Fauci held that thing up, I thought that should be in Rosa's office. So we think exactly the same way.

Let me first go to Dr. Collins. A couple of my colleagues have raised, and I think very appropriately, concerns about China. But, look, we know China is sort of a bad actor. They will steal anything that is not nailed down. And we have plenty of evidence of them trying to penetrate our research within the biomedical sphere in particular.

So I would like you to take a moment and tell us what you are doing in response to that? What are the things that, you know, are underway at the NIH to make sure that our intellectual property is safe and, frankly, that science is used in an appropriate way, which I think our people at the NIH do? I am not sure what the Chinese counterparts always do as well. I don't mean that individually. I mean that in a regime way.

Dr. COLLINS. Well, I appreciate the question. This is a very serious issue and one where we, the NIH, are out in front of all the science agencies in trying to be sure that our resources are not

being misused and intellectual property being appropriated inappropriately to another country.

First of all, let me say that we depend for the success of the American scientific enterprise on a broad diversity of folks who come to our country from other places and contribute wonderfully to progress, including winning Nobel Prizes. And I want to be really clear that the vast majority of those foreign-born scientists are wonderful additions to our community that we greatly value.

But there are some bad actors. We have been very aggressive in seeking those out, finding examples of individuals. And, yes, most of them are from China, who have been supported through something called the Thousand Talents program or similar programs like that from China where they basically have deceived us in terms of the support they have for their work from the Chinese Government and, in some instances, have in fact been diverting intellectual property as a result.

We have acted on that. We have worked with the FBI. There have been at least 80 instances of individuals who have quickly resigned or been terminated, and there are criminal actions that have been undertaken in some instances. So I think we are taking this with a grain of seriousness in watching for other examples. I think nobody at this point would imagine that we are looking the other way. We are looking really carefully to try to identify if there are people who are misusing the resources that we provide them and that we will not allow that to continue.

Mr. COLE. Well, I very much appreciate that and commend you for your diligence and urge you to double down on that.

Now, Dr. Fauci, if I could turn to you very quickly, I am very interested in the efforts on tick-borne research. One of our best supporters who is not on this committee is our good friend from New Jersey, Chris Smith. That has been an interest of his, and, honestly, I appreciate his advocacy for this program. So I want to give you a chance to update us on that.

Dr. FAUCI. Yeah. Thank you very much for that question, Congressman Cole. We actually, as you probably know, the HHS has a Tick-Borne Disease Working Group, which we are now coordinating work not only at the NIH but also with the CDC and other agencies to address tick-borne disease.

Particularly, one that is particularly problematic, as you well know, is Lyme disease. We still have what I believe is not yet an adequate vaccine to be able to be used. We had one vaccine early on that was not used probably because of, I think, some ill-advised concern that was not really justified about the toxicity of the vaccine, which it really was not. So we are going to be starting all over again to try and do that.

There are a number of other things also looking at how you can block transmission by inhibiting proteins in the ticks that actually transmit it. So there are four or five other things that are going on right now. So we are taking that very seriously because, as we all know, tick-borne disease, particularly Lyme disease, is of concern as you get into the post-Lyme syndrome, which is something that is bothersome not only to individuals but actually to communities as a whole where you have a lot of Lyme disease in a community.



Mr. COLE. Thank you very much.

Dr. FAUCI. So we are on it.

Mr. COLE. I Appreciate that. Madam Chair, thanks for the indulgence on the time. I yield back.

The CHAIR. Thank you.

Congresswoman Roybal-Allard.

Ms. ROYBAL-ALLARD. Dr. Collins, according to a 2019 Survey USA nationwide poll, 80 percent of voters said that medical researchers seeking funding for animal tests should first be required to show that an alternative is not available. Unfortunately, this is not always the case. The OIG reports have repeatedly found that failure to search for alternatives to pain procedures and to document the availability of alternatives in research proposals is common, and scientists who have served on laboratory oversight committees have echoed this concern.

I am going to ask all three questions in the hope that I can get to Dr. Volkow. What role has NIH played in educating the research community about non-animal research methods? What steps is NIH taking to incentivize researchers to utilize existing human non-animal approaches? And have you offered any training grants or any stage investigator or warrants or supplementary grant funding to give researchers the resources and confidence needed to switch from an animal-based to animal-free research method?

Dr. COLLINS. Well, very quickly, because I know you want to ask another question, we are very much interested in trying to be sure that every experiment that involves animals is done appropriately with rigor and reproducibility and that the animal model is, in fact, one that is going to give valuable information for human health. In many instances, there really are no alternatives to the animal model to be able to get those answers, and so we need to support that to be sure we are doing it, though, with great responsibility.

In terms of grants to others, yes, we are supporting vigorously such things as tissue chips, which allow you to look at the effect of a drug or some other intervention in a chip. And it is basically made up of human cells, maybe closer to humans, but that doesn't work for lots of other applications. So we still are going to need animals. But we are looking at this as vigorously as we can, looking forward to a time where we have more substitutions.

I think, though, to be honest, for the foreseeable future, if we are going to make advances in things like cancer, diabetes, heart disease, rare diseases, we are still going to need to depend for a lot of that effort on animal research.

Ms. ROYBAL-ALLARD. Well, I look forward to working with you on this issue. I will be introducing a bill, which I would like to talk to you about later.

Dr. Volkow, the last time we met, you were starting to do some research on marijuana. Can you give us an update on the research that you are doing and the impact of marijuana on the brain, especially the developing brain?

Dr. COLLINS. We are not hearing.

Dr. VOLKOW. Research on marijuana, and one of the most prominent ones is [inaudible] targeted towards understanding in a longitudinal study in a large sample size of children how exposure to marijuana may influence the development of the brain, how it may

influence cognition and behaviors, and how ultimately it may affect their performance at school. That study is ongoing and already has resulted in publications that, for example, show that the use of marijuana during pregnancy was associated with delayed development of the newborn brain.

But this is not the only project that we are doing. We are actually very interested also on establishing better ways of standardizing the metrics of consumption so that when people look at whether it is for medical purposes or to understand negative consequences, what are the doses that people are being exposed to? So, yes, we have not neglected at all this area of research. It is extremely important.

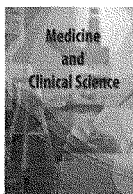
Ms. ROYBAL-ALLARD. I see my time is up. Thank you so much.

The CHAIR. Congressman Harris.

Mr. HARRIS. Thank you very much. And, first, I just want to—just to correct the record. I think Mr. Pocan paraphrased what my question was about the Wuhan Institute. It did not have to do with globally not funding overseas research. It had to do with through the indirect costs that are associated with grants actually sending money to the Wuhan Institute of Virology when we don't know if they are doing gain of function research.

Now, Dr. Collins, although you do mention that Moderna might not have had a problem with the transfer of IP to other countries regarding vaccines, I will tell you that the CEO of Pfizer certainly had a different opinion, and the CEO of BIO, the Biotechnology Innovation Organization, certainly has a different opinion about that effect. And I would ask unanimous consent to enter their statements into the record that oppose the transfer of intellectual property to other countries.

[The information follows:]



## International Reference Pricing in Congressional Bill H.R.3 and Its Potential Impact on the U.S. Biotech Ecosystem

Duane Schulthess

Vital Transformation, LLC, Washington, DC, USA

### Correspondence

Duane Schulthess, MBA,

Vital Transformation, LLC, 80 M St SE, First Floor, Washington, DC, 20003, USA

E-mail: duane.schulthess@vitaltransformation.com

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### Abstract

The U.S. Congress has proposed reference pricing for Medicare Part D under Congressional Bill H.R.3 with the objective of benchmarking U.S. drug pricing against an average price basket of 11 countries for the 125 drugs with the greatest net spending in the United States. U.S. drug prices were found to be 3.7 times higher on average.

This study identifies 69 medicines that would be affected by international reference pricing under H.R.3, representing 70% of Medicare Part D spending. We calculate that implementing H.R.3 would lower overall industry revenue by \$71.6 billion a year, a reduction of 58% in earnings before interest and taxes (EBIT) revenue.

The industry spends over \$60 billion a year investing in partnerships, development agreements, and acquisitions with innovative biotech firms. The revenue reductions caused by H.R.3 would directly impact the free cash flow available for these agreements.

We investigated the historical investments of large pharma companies impacted by H.R.3 into 85 lead assets of biopharma companies in California – that state received the largest share of commercial investments between 2009 and 2019. We show that the total sum of the investments per lead product is a statistically significant predictor of annual product revenue ( $p < 0.0001$ ).

We also used a logistic probability model ( $p < 0.0001$ ) to test the impact of a 58% reduction in revenue on market entry under H.R.3, finding a greater than 80% reduction in the number of drugs that would be brought to market by California biopharma companies owing to changed investor behavior and reduced firm-level liquidity.

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### Introduction

Since the election of President Trump and his promise that, "I'm going to bring down drug prices" [1], there have been several U.S. government initiatives aimed at controlling the price of medicines under Medicare Parts B and D. On October 26, 2018, Alex M. Azar II, Secretary of Health and Human Services (HHS), said that the government was to use an international average price for drugs paid by a basket of countries to determine a U.S. average "reference price." That price would be set as a benchmark against which to peg the prices of drugs under Medicare Part B; we calculated and presented the projected impact of that policy in a previous analysis [2].

Following the reference pricing plan of HHS, the U.S. Congress in 2019 proposed its own version of reference pricing for Medicare Part D, known as bill H.R.3: the Lower Drug Costs Now Act of 2019 [3]. Unlike the limited scope of Secretary Azar's plan, which encompasses 21 drugs, H.R.3 targets the 125 drugs for which there was an estimated greatest net spending in the 50 United States, the District of Columbia, and their territories "during the most recent plan year prior to such drug publication date for which data are available." [4] In contrast to the Medicare

Part B reference pricing proposal by the HHS, the stated goal of H.R.3 is to reduce pricing throughout the entire U.S. commercial market for the 125 therapies with the highest cost to Medicare Part D.

Specifically, the core objective of H.R.3 is to force U.S. drug prices down to the average of prices paid in a basket of 11 countries, a metric called the Average International Market (AIM) price. The House Ways and Means Committee commissioned research conducted by So-Yeon Kang et al. [5] that compared drug prices in the United States to those in the United Kingdom, Japan, Ontario (Canada), Australia, Portugal, France, the Netherlands, Germany, Denmark, Sweden, and Switzerland to determine the price differences between the markets.

Altering the pricing and revenues of the 125 most sold drugs in the U.S. could have profound effects on the current biopharma ecosystem. One of those effects would be a substantial decrease in free cash flow by \$71.6 billion per year available to invest in development agreements, partnerships, and acquisitions with innovative biotech firms. As a case in point, from 2009 to 2019, 25 companies potentially impacted by H.R.3 invested \$621 billion in such agreements with U.S.-based biotech firms.

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**Table 1.** Impact of H.R.3 at the firm level, accounting for a new AIM reference price substituting for 2017 sales; the total impact highlighted is \$71.6 billion dollars of net revenue per year

| Company   | Number of Drugs | Reference Discount | US Total Sales 2017 (\$US Mil) | Revised Total Sales (\$US Mil) | Revised Total Sales Pelosi 1.2 Margin (\$US Mil) | Change In Revenue (\$US Mil) | Total R&D Spend 2017 (\$US Mil) | Reduction as a % of R&D (\$US Mil) | Reduction as 20% R&D ratio (\$US Mil) |
|-----------|-----------------|--------------------|--------------------------------|--------------------------------|--------------------------------------------------|------------------------------|---------------------------------|------------------------------------|---------------------------------------|
| Company S | 2               | 73%                | \$14,505                       | \$3,965                        | \$4,758                                          | -\$9,747                     | \$5,007                         | -195%                              | -39%                                  |
| Company C | 5               | 77%                | \$8,719                        | \$2,016                        | \$2,419                                          | -\$6,300                     | \$3,925                         | -161%                              | -32%                                  |
| Company E | 3               | 83%                | \$6,479                        | \$1,129                        | \$1,355                                          | -\$5,124                     | \$2,254                         | -227%                              | -45%                                  |
| Company F | 2               | 73%                | \$6,580                        | \$1,801                        | \$2,161                                          | -\$4,419                     | \$3,562                         | -124%                              | -25%                                  |
| Company G | 6               | 57%                | \$9,032                        | \$3,883                        | \$4,659                                          | -\$4,373                     | \$3,734                         | -117%                              | -23%                                  |
| Company Q | 6               | 69%                | \$6,563                        | \$2,025                        | \$2,429                                          | -\$4,134                     | \$9,143                         | -45%                               | -9%                                   |
| Company D | 2               | 70%                | \$6,434                        | \$1,942                        | \$2,331                                          | -\$4,103                     | \$3,274                         | -125%                              | -25%                                  |
| Company K | 5               | 78%                | \$5,518                        | \$1,200                        | \$1,440                                          | -\$4,078                     | \$5,357                         | -76%                               | -15%                                  |
| Company H | 4               | 73%                | \$6,023                        | \$1,654                        | \$1,985                                          | -\$4,038                     | \$4,894                         | -83%                               | -17%                                  |
| Company B | 4               | 83%                | \$4,711                        | \$779                          | \$935                                            | -\$3,776                     | \$3,078                         | -123%                              | -25%                                  |
| Company R | 3               | 74%                | \$4,879                        | \$1,254                        | \$1,505                                          | -\$3,374                     | \$7,645                         | -44%                               | -9%                                   |
| CompanyM  | 4               | 84%                | \$3,790                        | \$590                          | \$708                                            | -\$3,082                     | \$9,818                         | -31%                               | -6%                                   |
| Company P | 3               | 56%                | \$5,655                        | \$2,506                        | \$3,008                                          | -\$2,647                     | \$14,014                        | -19%                               | -4%                                   |
| Company I | 2               | 79%                | \$3,400                        | \$708                          | \$850                                            | -\$2,550                     | \$4,482                         | -57%                               | -11%                                  |
| Company U | 3               | 76%                | \$3,448                        | \$844                          | \$1,012                                          | -\$2,436                     | \$8,510                         | -29%                               | -6%                                   |
| Company J | 4               | 57%                | \$4,834                        | \$2,057                        | \$2,468                                          | -\$2,366                     | \$5,472                         | -43%                               | -9%                                   |
| Company O | 1               | 65%                | \$1,331                        | \$470                          | \$564                                            | -\$768                       | \$1,957                         | -39%                               | -8%                                   |
| Company L | 1               | 71%                | \$1,133                        | \$329                          | \$394                                            | -\$739                       | \$1,326                         | -56%                               | -11%                                  |
| Company W | 1               | 71%                | \$1,120                        | \$327                          | \$392                                            | -\$728                       | \$2,108                         | -35%                               | -7%                                   |
| Company X | 2               | 78%                | \$829                          | \$186                          | \$223                                            | -\$606                       | \$5,455                         | -11%                               | -2%                                   |
| Company T | 2               | 85%                | \$733                          | \$109                          | \$130                                            | -\$602                       | \$2,930                         | -21%                               | -4%                                   |
| Company N | 1               | 71%                | \$826                          | \$239                          | \$287                                            | -\$538                       | \$1,161                         | -46%                               | -9%                                   |
| Company Y | 1               | 74%                | \$662                          | \$171                          | \$205                                            | -\$457                       | \$10,529                        | -4%                                | -1%                                   |
| Company A | 1               | 71%                | \$666                          | \$193                          | \$232                                            | -\$434                       | \$361                           | -120%                              | -24%                                  |
| Company V | 1               | 71%                | \$377                          | \$109                          | \$131                                            | -\$246                       | \$1,991                         | -12%                               | -2%                                   |
| TOTAL     | 69              | 72%                | \$108,246                      | \$30,484                       | \$36,581                                         | -\$71,665                    | \$120,920                       | -59%                               | -12%                                  |

## Materials and methods

In September of 2019 the House Ways and Means Committee published the results of its pricing study, entitled “A Painful Pill to Swallow: U.S. vs. International Prescription Drug Prices” [6]. Its core findings were as follows: “U.S. drug prices were nearly four times higher than average prices compared to similar countries ... individual drug prices in the U.S. ranged from 70 to 4,833 percent higher than the combined mean price in the other 11 countries. On average, U.S. drug prices were 3.7 times higher than the combined average of the other 11 countries in the study” [6].

Based on the House Ways and Means Committee analysis, Vital Transformation identified 69 medicines sold by 25 companies that would be affected by international reference pricing under H.R.3. These 69 medicines account for roughly 70% of 2019 Medicare Part D spending.

Using the 2017 per-dose pricing taken from the Medicare Part D Spending Dashboard [7], we calculated for each of the 25 firms the revised Medicare Part D revenue using the new H.R.3 reference price for their respective medicines. The 2017 U.S. product revenue per firm was extracted from the firms’ audited annual reports, SEC 10-K filings, and the Pharma Intelligence database Medtrack (Table 1).

For example, in Table 1, we observe that Company S, which has two therapies impacted by the AIM index, would see a reduction in its 2017 revenues from \$14.5 billion to \$4.8 billion—a drop of \$9.7 billion per year. As that company currently spends \$5 billion a year on R&D, a loss of revenue at this level would have an enormous impact on its future R&D activities. In addition, since the industry historically spends over \$60 billion a year investing in partnerships, development agreements, and acquisitions of smaller innovative biotech firms, this revenue reduction would have profound repercussions on how Company S uses its free cash flow to invest in such initiatives. Increasingly, this is how the life sciences sector is moving innovative products quickly from research to market.

In total, H.R.3 reduces revenues of 25 companies with impacted Medicare Part D products by \$71.6 billion per year. While this finding is significant in and of itself, we see that the impact is even greater on firms that have more than one Medicare Part D product impacted by the AIM price index. As the legislation is based on price assessments at the product level, the more products a firm has, the greater on average will be the reduction in that firm’s revenues.

Putting the reduced revenues caused by H.R.3 into context, the global net earnings before income tax (EBIT) of the 25 companies in our analysis that are impacted by H.R.3 were \$124.2 billion in 2017.

**Table 2.** 23 products approved from 2009 - 2019 that received inward or outward California partnership revenue, licensing, or acquisitions from H.R.3-impacted companies, and the total net revenues earned by those products in 2017

| Lead Product Name  | Total Invested (million) | 2017 Revenue (million) |
|--------------------|--------------------------|------------------------|
| Sovaldi            | \$11,000                 | \$4,370                |
| Kyprolis           | \$10,400                 | \$1,397                |
| Pirfenidone        | \$8,300                  | \$1,647                |
| Bydureon           | \$7,000                  | \$1,042                |
| Lokelma***         | \$2,700                  | \$14                   |
| Kybella            | \$2,100                  | \$106                  |
| Stuganon           | \$1,695                  | \$0                    |
| Lesimurad          | \$1,260                  | \$2                    |
| Zydelig            | \$1,200                  | \$149                  |
| Inrebic***         | \$1,200                  | \$11                   |
| Blinexyto          | \$1,160                  | \$289                  |
| Bevespi Aerosphere | \$1,150                  | \$16                   |
| Erleada            | \$1,000                  | \$248                  |
| OncoVEX            | \$1,000                  | \$0                    |
| Quillivant XR      | \$680                    | \$0                    |
| Nimotuzumab        | \$510                    | \$0                    |
| Quizaritinib       | \$465                    | \$0                    |
| Relovair           | \$342                    | \$1,269                |
| Parsabiv**         | \$315                    | \$389                  |
| Otiprio            | \$133                    | \$1                    |
| Mepsevii           | \$75                     | \$0                    |
| Laninamivir        | \$46                     | \$0                    |
| Lonhala Magnair    | \$30                     | \$13                   |

\*\*Revenue taken from 2018  
\*\*\*Revenue taken from 2019

A reduction of \$71.6 billion in net revenue represents a loss in net earnings of 58% for the biopharma sector at large. This significant drop in net earnings is in line with the non-partisan Congressional Budget Office's (CBO) estimate of Medicare Part D savings of \$336 billion over five years [8].

Further, while the assumption is that H.R.3 prices will only impact Medicare Part D revenues, the reality is that Medicare Part D uses the same pharmaceutical benefit managers (PBMs) as the commercial market to negotiate pricing. It would be impossible to wall off a 70% price reduction in Medicare Part D from the overall commercial market; all prices would fall and the entire commercial market would be impacted.

To understand the wider impact of a 58% drop in net revenue, from October 2009 to 2019, biopharma firms invested a total \$621 billion of funding into biopharma partnerships, licensing agreements, and acquisitions in the U.S. Of those investments, California attracted the largest share—approximately 30% (\$178 billion), accounting for both inward and outward investments to and from the state. In total, 85 firms received investments into their lead products, of which 23 came to market as a result of these investment partnerships in California.

As we estimate the impact of H.R.3 on free cash flow for investment partnerships and development to be a reduction of 58%, we also aim to determine how accurate the industry is at predicting the future revenue and cash flow of these lead assets. In this way, we

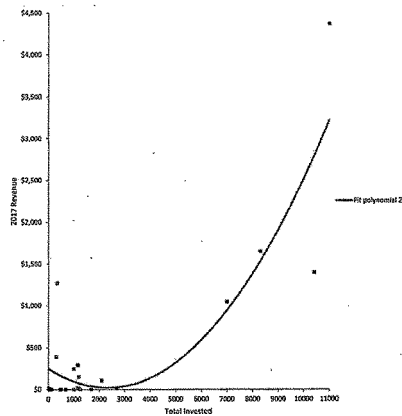


**Figure 1.** Regression testing 2017 revenue predicting total investments into 23 marketed assets,  $p < 0.0001$ .

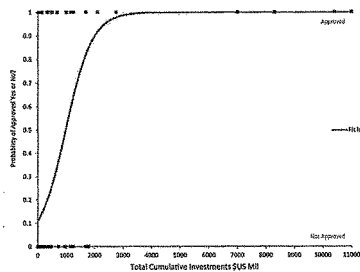


**Figure 2.** Logistic probability for a given level of investment from 2009 to 2019 into 81 lead products of emerging Californian biotech firms, 23 products gaining approval for marketing authorization,  $p < 0.0001$ .

can calculate the projected impact of reduced revenue on investment behavior and the probability of an asset's market entry.

Investments are made in advance of market entry of a product, often years ahead of its approval. Yet, there appears to be a relationship between the size of the financial commitment made to a product and the annual revenue it generates once the product is authorized. Thus, if the relationship between future revenue and investment size proves to be statistically significant, we can estimate the impact of reduced revenues on partnerships with H.R.3-impacted firms.

An often-heard criticism of the current biopharma development model is that investors backing new and emerging assets are overpaying, thus needlessly driving up costs and taking on unjustifiable risks for a given asset. To assess this critique and to test whether the relationship between investments and revenue is

**Table 3. Impact of reduced revenues on market entry on 23 Californian biotech assets under two U.S. House of Representatives international pricing proposals**

| Drug Name          | Total Investment (\$24 bl) (\$USD Bn) | Current Probability | Ways and Means Revised Revenue (\$35 bl Available Capital) | H.R. 3 Total Market Impact (\$23 bl Available Capital) |
|--------------------|---------------------------------------|---------------------|------------------------------------------------------------|--------------------------------------------------------|
| Sovkafinonem       | \$11,000                              | 100.00%             | 100.00%                                                    | 99.96%                                                 |
| Kyprollis          | \$10,400                              | 100.00%             | 100.00%                                                    | 99.93%                                                 |
| Pirfenidone        | \$8,300                               | 100.00%             | 99.99%                                                     | 99.56%                                                 |
| Bydureon           | \$7,000                               | 100.00%             | 99.96%                                                     | 98.58%                                                 |
| Lokelma            | \$2,755                               | 97.80%              | 86.15%                                                     | 99.91%                                                 |
| Kytbella           | \$2,100                               | 91.66%              | 71.03%                                                     | 45.25%                                                 |
| Sugenon            | \$1,695                               | 82.22%              | 57.95%                                                     | 36.43%                                                 |
| Lesinurad          | \$1,260                               | 64.61%              | 42.61%                                                     | 27.89%                                                 |
| Zydelig            | \$1,200                               | 61.63%              | 40.54%                                                     | 26.81%                                                 |
| Inrebic            | \$1,200                               | 61.63%              | 40.54%                                                     | 26.81%                                                 |
| Bilincryo          | \$1,160                               | 59.59%              | 39.18%                                                     | 26.11%                                                 |
| Bevespi Aerosphere | \$1,150                               | 59.08%              | 38.84%                                                     | 25.53%                                                 |
| Erlada             | \$1,000                               | 53.17%              | 33.91%                                                     | 23.41%                                                 |
| OncoVEX            | \$1,000                               | 53.17%              | 33.91%                                                     | 23.41%                                                 |
| Quilivant XR       | \$680                                 | 34.60%              | 24.56%                                                     | 18.63%                                                 |
| Nimotuzumab        | \$510                                 | 26.90%              | 20.36%                                                     | 16.41%                                                 |
| Quizartinib        | \$465                                 | 25.05%              | 19.34%                                                     | 15.86%                                                 |
| Relovalir          | \$342                                 | 20.46%              | 16.76%                                                     | 14.43%                                                 |
| Parsabiv           | \$335                                 | 19.52%              | 16.23%                                                     | 14.13%                                                 |
| Onpattro           | \$333                                 | 14.13%              | 13.02%                                                     | 12.25%                                                 |
| Mepsevir           | \$75                                  | 12.69%              | 12.10%                                                     | 11.70%                                                 |
| Laninamivir        | \$46                                  | 12.02%              | 11.67%                                                     | 11.49%                                                 |
| Lonthala Magnair   | \$30                                  | 11.66%              | 11.44%                                                     | 11.26%                                                 |
| BRING TO MARKET    |                                       |                     | DO NOT BRING TO MARKET                                     |                                                        |

statistically significant, we ran a polynomial regression comparing the annual revenue in 2017 with the total investments made over 10 years (Table 2). The goal of the regression was to assess the model's accuracy in retroactively predicting the total size of those investments based solely upon 2017 revenues (Figure 1, Data table 1 in Appendix).

The result indicates that the relationship between investments and future annual revenues is statistically significant ( $p < 0.0001$ ). As well, the estimated relationship explained by the regression between investments and revenues accounts for 77% of the model's variability ( $R^2 = 0.773$ ).

In essence, what the model shows is that investors are sensitive to the revenue potential of new therapies and dedicate the most capital to those assets with the greatest probability of generating liquidity. In consequence, a potential future 58% cut in net revenues from free cash flow due to H.R.3 would have substantial implications for their willingness to invest in higher-risk, lower margin products.

The key question then is how many assets would not be brought to market as they would be no longer economically viable under H.R.3 revenue reductions?

To answer that question, we used a logistic regression to model the probability of market entry for 81<sup>1</sup> products invested through Californian biotech partnerships from 2009 to 2019, based on the total investment they received (Figure 2, Data table 2 in Appendix). The result shows that the total amount invested in a firm is a statistically significant predictor of successful market entry, and the point at which a firm has a 50/50 probability of market entry is at an investment of roughly \$1 billion.

## Results

Given that our logistic regression represents a probability model for market entry for a given level of investments, we can use the probability logit function equation to test the impact of revised revenues on the likelihood of an asset's market entry as a function of the decision to invest. We modeled two scenarios: the impact of the House Ways and Means Committee's proposal on Medicare Part D, and the full AIM impact on the commercial market – including a 20% “fair price” margin allowed under H.R.3 (Table 3).

\*For the purpose of this analysis, we have removed the classes of ophthalmology and dermatology investments to keep the analysis focused on innovative treatments for areas of high unmet medical needs.

Investors will still need to invest in clinical research to understand the revenue potential of a given asset, and the threshold for that investment as determined by our logistic regression model (Figure 2) is roughly \$1 billion for a 50/50 probability of market entry. This will continue to be a fixed cost per asset, as none of the provisions under H.R. 3 target regulatory reform.

The average rate of market entry in biopharma for new assets is a 9% success/91% failure ratio [9]. Under H.R.3, competition for the most promising assets would likely not reduce the cost of acquisitions, and productivity in pharmaceutical R&D also continues to decline [10] as development costs continue to increase. Given these facts, it is axiomatic that any reduction in revenue caused by H.R.3 would lead to fewer assets receiving investments. As the failure rates of clinical research are above 90%, this impact will be nonlinear.

When modeling the full impact of H.R.3, which reduces the available investment capital in the Californian biopharma market from \$54 to \$23 billion, we find the market entry for new products similarly shrinks from 23 to 5, all things being equal and assuming only those assets with a positive probability will remain investable. Under the revised scenario, no longer approved would be treatments for cancer, non-insulin-dependent diabetes, chronic obstructive pulmonary disease (COPD), and novel treatments for gout, bronchitis, and emphysema.

Also concerning is the fact that our cohort would lose orphan drugs for rare conditions with no other treatment options, including therapies for pediatric hyperparathyroidism, Sly syndrome, and bone cancer.

## Discussion

H.R.3 specifies that the AIM price, that is the international average price, can be raised to what is called a “fair price,” which “shall not exceed 120 percent of the AIM price applicable to such drug with respect to such year” [11]. Yet, the average AIM discount in our cohort of 69 drugs is a 72% reduction from the current price; a 20% “fair” margin added back to the AIM price would yield only an additional 6% in revenue when compared with the unadjusted 2017 price. In other words, the revenue reduction in the AIM price of 72% is so large that a 20% increase from the new reduced base would be negligible.

What H.R.3 ignores are several key facts about the way our

biopharma system actually works. Mainly, the way the bill is drafted seems to assume that biopharma innovation occurs internally in a closed R&D environment. This is not the case.

Increasingly, the pharmaceutical industry specializes in partnering with innovative small, emerging biotech firms and carrying their most promising new assets over the phase III finish line for commercialization internationally. Both undertakings are very demanding in terms of human and material resources, time, and costs. As small biotech firms are not staffed and built to commercialize assets, the barriers under the current regulatory structures are far too onerous for them to manage alone.

In the view of Ithai Stern, professor of strategy at the Kellogg Business School, "For these tiny biotech firms, forming partnerships is everything. Their success depends heavily on their ability to build relationships with established companies—and in many cases, the earlier, the better" [12]. Indeed, the optimum solution for small biotech firms is often to partner with a bigger pharmaceutical company and license assets for commercialization or eventual acquisition.

### Conclusions

H.R.3 is one of several legislative proposals related to drug pricing. As mentioned earlier, HHS is also promoting the International Pricing Initiative for Medicare Part B, which alone would reduce net revenue by \$15 billion a year, amounting to a total annual reduction of \$87 billion for the industry for both proposals. The combined impact of these bills would be catastrophic to the U.S. innovative biotech sector, which has been a growth engine for the U.S. economy. For example, California doubled employment in biotech R&D from 21,000 to 44,000 people over the ten-year period of our cohort analysis [13].

According to HHS Secretary Alex M. Azar II, "[Reference pricing assumes] that companies cannot drive somewhat higher prices in Europe and Japan, which they almost certainly can do" [14]. In fact, most companies operating in the EU are under severe pressure to lower their current pricing, and have been facing increasing threats that governments will confiscate their IP under the World Trade Organization allowances for compulsory licensing [15].

A far more likely scenario is that companies with exposure to H.R.3 would simply "slow-walk" any new drug approval in Europe, or even avoid releasing the therapy in any country where they are AIM benchmarked at all, rather than risk their U.S. profit margin. This means that those in need of new treatments in Europe would likely not gain access until a generic treatment becomes available.

In 2015, Vital Transformation held an international conference with 200 thought leaders in the U.S. capital, co-sponsored by 21st Century Cures, where we discussed adaptive licensing and adaptive reimbursement for new medicines [16]. An adaptive pathway harnessing real world evidence could theoretically reduce the time to market by half, radically impacting the capital requirements for drug discovery while stimulating the market to increase competition, thus lowering costs.

Perhaps it is time to have another look at adaptive licensing and reimbursement. Punitive measures such as H.R.3 would either devastate available cash flow by over 50% and radically impact pipelines or leave Europeans with untreated medical conditions without access to effective innovative medicines.

### Funding statement

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Appendix

Data table 1 – Regression values underlying the model in Figure 1

|                                  |                                                                         |           |              |            |       |         |
|----------------------------------|-------------------------------------------------------------------------|-----------|--------------|------------|-------|---------|
| Fit                              |                                                                         |           |              |            |       |         |
| N                                | 23                                                                      |           |              |            |       |         |
| Mean of Y                        | 476.698696                                                              |           |              |            |       |         |
| Equation                         | 2017 Revenue = 253.7 - 0.2007 Total Invested + 4.28e-05 Total Invested² |           |              |            |       |         |
| R²                               | 0.773                                                                   |           |              |            |       |         |
| R² adjusted                      | 0.750                                                                   |           |              |            |       |         |
| RMSE                             | 494.546152                                                              |           |              |            |       |         |
| Parameter                        | Estimate                                                                | 95% CI    |              | SF         | t     | p-value |
| Constant                         | 253.7                                                                   | -99.53    | to 606.9     | 169.33     | 1.50  | 0.1497  |
| Total Invested                   | -0.2007                                                                 | -0.5107   | to 0.1093    | 0.14860    | -1.35 | 0.1920  |
| Total Invested²                  | 4.280E-05                                                               | 1.350E-05 | to 7.210E-05 | 1.4046E-05 | 3.05  | 0.0064  |
| H0: β = 0                        |                                                                         |           |              |            |       |         |
| The parameter is equal to 0.     |                                                                         |           |              |            |       |         |
| H1: β ≠ 0                        |                                                                         |           |              |            |       |         |
| The parameter is not equal to 0. |                                                                         |           |              |            |       |         |

Effect of Model

| Source     | SS         | DF | MS         | F     | p-value |
|------------|------------|----|------------|-------|---------|
| Difference | 16669699.6 | 2  | 8334849.81 | 34.08 | <0.0001 |
| Error      | 4891517.93 | 20 | 244575.897 |       |         |
| Null model | 21561217.6 | 22 | 980055.343 |       |         |

H0:  $E(Y|X=x) = \mu$   
The model is no better than a null model  $Y=\mu$ .  
H1:  $E(Y|X=x) = \beta_0 + \beta_1x + \beta_2x^2$   
The model is better than the null model.

Data table 2 - Logistic Regression values underlying the model in Figure 2

Fit

|           |          |          |             |            |  |
|-----------|----------|----------|-------------|------------|--|
| N         | 81       |          |             |            |  |
| Parameter | Estimate | 95% CI   |             | SE         |  |
| Constant  | -2.089   | -2.894   | to -1.285   | 0.41051    |  |
| Total     | 0.002136 | 0.001017 | to 0.003255 | 5.7095E-04 |  |

$\beta = \log \Phi_1$

Effect of Model

|              |                |    |                          |         |
|--------------|----------------|----|--------------------------|---------|
| Source       | Log-likelihood | DF | G <sup>2</sup> statistic | p       |
| Difference   | 15.127         | 1  | 30.25                    | <0.0001 |
| Fitted model | 33.202         | 79 |                          |         |
| Null model   | 48.328         | 80 |                          |         |

H0:  $g(x) = \beta_0$   
The model is no better than a null model  $Y=\pi$ .  
H1:  $g(x) = \beta_0 + \beta x$   
The model is better than the null model.

The data set used in this analysis is available at the following link:  
<https://1drv.ms/x/s!AGuTWbx7xz9yAHMUzdp5Rfm5NFm?e=4GVpRf>



Mr. HARRIS. I am also concerned, Dr. Collins, because you are, you know, the researcher general of the country, that you would—I hope that you will take the position on the effect of H.R. 3, if it should become law, on the negative impact it would have on research. And I would ask unanimous consent to enter into the record a report from Vital Transformations, a group that would report on the devastating effect it would have on biotechnology research going forward since so much of our biotechnology research is funded by private companies, not by the NIH.

Madam Chair, I ask unanimous consent that they be entered into the record.

The CHAIR. So ordered. Sorry. So ordered.

Mr. HARRIS. Thank you. Now, two other—just two very quick things. One is, is that I do worry about therapeutics. And, you know, we seemed to have solved the vaccine problem, but therapeutics are an issue because if variants become prevalent and our vaccines don't work against the new variants, therapeutics will be important.

And I was a little concerned that BARDA has suddenly suspended their broad agency announcement. Of course, you know, the NIH is not BARDA, but there was no public explanation why, and some unofficial discussions indicated that the funding was being channeled to NIH. So I would hope that NIH and, Dr. Collins, that you share my concern for the vital importance of the private sector in funding our biotechnology research.

And just a final question for Dr. Volkow. Just put plainly, is recreational use of marijuana in youth with a still developing brain a good idea?

Dr. VOLKOW. No.

Mr. HARRIS. Okay. So there is no new research that shows somehow because there is an acceleration among States of legalizing recreational marijuana, but there is no research that would indicate, new research, that it is actually not a bad thing. Is that right? There is no new research indicating that it is good for developing brains, for instance.

Dr. VOLKOW. There is no research indicating that it is benign in young people, but there is increasing research indicating that it has deleterious effects.

Mr. HARRIS. Okay. Thank you very much, and I yield back the few remaining seconds I have, Madam Chairman.

The CHAIR. Okay. Yes.

Congresswoman Lee.

Ms. LEE. Chairman, this has been such an informative hearing, but, also, it gives me a lot of hope. It is truly life affirming, all of the work that you do.

And I wanted to follow up with Dr. Gibbons on so many of the issues that we have been working with over the years because it relates to diseases that I have personal knowledge of that NIH has been so helpful in putting on the radar and conducting research. One is our COPD action plan. You all know my late mother died from complications of COPD, and I would like to know where we are with our COPD plan.

Secondly, with the issue of multiple sclerosis, again, the research, where we are on MS in terms of a cure. And, of course,

many of you know my sister has MS, and I have worked on this issue for many, many years.

Finally, Dr. Gibbons, the whole issue around sickle cell disease, where we are in terms of a cure, and have we figured out how to address the sickle cell trait as it relates to HIV—excuse me—as it relates to diabetes and how to identify those most, you know, prone to sickle cell trait and the A1C test.

Dr. GIBBONS. Well, thank you, Congresswoman.

Again, I appreciate your leadership in this area. And, again, in the spirit of your mom, we are making continued advances in COPD. Our Top Med program of precision medicine where we have sequenced over 150,000 individuals has been a key driver, and where we are starting to identify pathways that may be driving COPD. We hope that will usher in a new generation of therapeutics.

With regard to sickle cell, we are very excited about the opportunities. It is on the horizon to cure sickle cell disease. And we have made substantial progress in a number of trials now that are testing various curative genetic therapies that offer a lot of promise and have very encouraging preliminary results to suggest that we may be very much on the brink of a transformative kind of therapy to advance the lives of those living with sickle cell disease.

Critical to your point about sickle cell trait, that if, indeed, we have a curative therapy, it will be critical that there be genetic counseling to identify early on who is at most risk and, eventually could be cured from this disease. Thank you.

Ms. LEE. Thank you again.

Thank you, Madam Chair, very much.

Thank you all for this hearing.

The CHAIR. Thank you.

Ms. LEE. I yield back my time.

The CHAIR. Congresswoman Herrera Beutler.

Ms. HERRERA BEUTLER. Thank you, Madam Chair.

And, Dr. Volkow, just following up on what Dr. Harris was mentioning where you said you do see deleterious effects on the developing brain. To what age are brains developing, just so that I have an end point on that?

Dr. VOLKOW. Our brain does not stop developing until our mid-20s.

Ms. HERRERA BEUTLER. Okay. So people who are legally allowed to purchase recreational marijuana are still possibly developing, and it can have a deleterious effect on their brains.

Dr. VOLKOW. That is correct, and we are doing the studies to actually document how it negatively affects the brain.

Ms. HERRERA BEUTLER. Thank you. I wanted to ask, switching gears a little bit, in one of your blogs about the—and I am speaking fast to get it all in—monitoring our future survey for 2020, you—basically I wanted to see when we can expect to see results from the supplemental funds NIDA issued to research the impact of the pandemic on adolescence risk of substance use.

Dr. VOLKOW. We already are getting some of the results back. For example, one of the questions that we had was the extent to which the COVID pandemic was going to negatively influence vaping, which has been taken up so rapidly by teenagers. And

what the data seems to show is in some instances, when the parents are there at home, this has resulted in a decrease in vaping among teenagers overall. So that is one example.

But on the other hand, we are seeing negative effects, for example, of alcohol drinking or smoking in those families where the parents actually themselves take these drugs, or they are not at home to observe the behavior of these teenagers.

Ms. HERRERA BEUTLER. Got it. Thank you.

Dr. VOLKOW. We will get more data.

Ms. HERRERA BEUTLER. Thank you. I look forward to that.

I am going to switch over, I think over to Dr. Gibbons. Yes. So acute and chronic kidney disease in children are often—well, maybe—maybe, which doctor—in children often differs from that in adults, both in its underlying causes and its treatments. There are not enough pediatric nephrologists, not enough pediatric researchers. And we continue to struggle to obtain funding for research proposals, or at least the ones that are out there do. Without this funding, children with kidney disease are not able to benefit from the resources that Congress allocates to NIH and NIDDK.

So what is NIH doing to ensure that study sections have access to pediatric subspecialist reviewers who have the unique expertise required to review pediatric research proposals? And what other steps are you all taking to ensure research meets the needs of children with kidney disease?

Dr. Bianchi.

Dr. COLLINS. Dr. Bianchi is probably better positioned—

Dr. BIANCHI. Yes. So we have formed, actually, a trans-NIH Pediatric Research Consortium or N-PeRC, and that group meets every other month to discuss areas of shared interest. We happen to have a pediatric nephrologist on that committee. We also have a representative from the Center for Scientific Review. So the CSR knows that we are very interested in getting more pediatric reviewers onto the study sections. And by having a representative there, that person can hear what we are discussing. And we are particularly interested in adolescence, which is a gap area across NIH, and also the transition of adolescence to adulthood in terms of transferring their medical care. We have recently had a workshop on that whole issue. So it is a very active area of research.

Ms. HERRERA BEUTLER. Thank you. I yield back.

The CHAIR. Thank you.

Congressman Pocan.

Mr. POCAN. Thank you very much, Madam Chair.

Dr. Volkow, I have a question for you. In the last appropriations bill that we did, we added some language that said that the committee encourages NIDA to expand research on all health aspects of kratom. Specifically, we talked about people who may be abusing opioids, how it can help. We also directed some funds to the Agency for Healthcare Research and Quality, \$500,000 to do such, and we have had some promising results come back on that.

Just in the last month, the FDA did a major raid on a company in Florida on kratom using some old rhetoric that the FDA used to use in this area. I know there is no new guidance, there is no new head of FDA, but have you had any conversations with them? And there is also a letter that we just recently got access to from

2018 sent from the Secretary of HHS to DEA about kratom saying: Back off our early guidance. We were wrong. We need research on this.

Have you had any conversations with the FDA or anything we can do because I do think there is some really strong results for people who are getting addicted to opioids that can be help by kratom, and now we are seeing the opposite actions happening again under the FDA?

Dr. VOLKOW. We have not had discussions with the FDA during the COVID pandemic, but we did have them beforehand. We are very interested on the products, the chemicals that are within kratom, the most notable Mitragynine, which it has many interesting properties that could be of value potentially as medication for pain, but, also interestingly, it could also hold value as treatments for addiction. At the same time, we are aware that kratom can produce an addicition in some instances and that it can have toxicity. Therefore, highlights why this is important to actually do research on the substance that people are taking. They are taking it for multiple things.

Mr. POCAN. No. I appreciate that. If it would be possible, since the FDA doesn't have a technical head right now, to maybe reach out to them and let them know some of this because we really appreciate that great research work that you are advocating for right now. Thank you.

Dr. Collins, isn't it true, I believe you updated the report in the last year that in the last now, I believe it was, decade every single drug approved by the FDA had NIH research support. Is that correct?

Dr. COLLINS. That is correct. That was 100 percent of those drugs, and that was a study done by Dr. Fred Ledley and published in the Proceedings of the National Academy.

Mr. POCAN. Yeah. I have got that document, and, Madam Chair, without objection, I would like to enter that into the record as well.

[The information follows:]

# **Government as the First Investor in Biopharmaceutical Innovation: Evidence From New Drug Approvals 2010–2019**

**Ekaterina Galkina Cleary, Matthew J. Jackson, and  
Fred D. Ledley<sup>1</sup>**

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## **ABSTRACT**

The discovery and development of new medicines classically involves a linear process of basic biomedical research to uncover potential targets for drug action, followed by applied, or

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<sup>1</sup> Center for Integration of Science and Industry, Departments of Natural & Applied Sciences, Mathematical Sciences, and Management, Bentley University, Waltham MA. Corresponding author: Fred D. Ledley, Center for Integration of Science and Industry, Jennison Hall 143, Bentley University, 175 Forest Street, Waltham, MA 02452. Tel: 781.891.2046; email: [fredley@bentley.edu](mailto:fredley@bentley.edu). Center for Integration of Science and Industry at Bentley University [@sciindustry](http://www.bentley.edu/sciindustry)

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translational, research to identify candidate products and establish their effectiveness and safety. This Working Paper describes the public sector contribution to that process by tracing funding from the National Institutes of Health (NIH) related to published research on each of the 356 new drugs approved by the U.S. Food and Drug Administration from 2010-2019 as well as research on their 219 biological targets. Specifically, we describe the timelines of clinical development for these products and proxy measures of their importance, including designations as first-in-class or expedited approvals. We model the maturation of basic research on the biological targets to determine the *initiation* and *established* points of this research and demonstrate that none of these products were approved before this enabling research passed the *established* point. This body of essential research comprised 2 million publications, of which 424 thousand were supported by 515 thousand Funding Years of NIH Project support totaling \$195 billion. Research on the 356 drugs comprised 244 thousand publications, of which 39 thousand were supported by 64 thousand Funding Years of NIH Project support totaling \$36 billion. Overall, NIH funding contributed to research associated with every new drug approved from 2010-2019, totaling \$230 billion. This funding supported investigator-initiated Research Projects, Cooperative Agreements for government-led research on topics of particular importance, as well as Research Program Projects and Centers and training to support the research infrastructure. This NIH funding also produced 22 thousand patents, which provided marketing exclusivity for 27 (8.6%) of the drugs approved 2010-2019. These data demonstrate the essential role of public sector-funded basic research in drug discovery and development, as well as the scale and character of this funding. It also demonstrates the limited mechanisms available for recognizing the value created by these early investments and ensuring appropriate public returns. This analysis demonstrates the importance of sustained public investment in basic biomedical science as well as the need for policy innovations that fully realize the value of public sector investments in pharmaceutical innovation that ensure that these investments yield meaningful improvements in health.

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**JEL Codes:** G35, H1, H4, H5, L2, O3.

**Keywords:** innovation, basic research, translational science, technology transfer, NIH funding, Bayh-Dole, public policy, federal funding.

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## 1. Introduction

*“...the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition.”*

Constitution of the World Health Organization (WHO, 2006)

With these words, written in 1946, the post-war community of nations adopted the principle that health was a fundamental human right. The document went on to charge governments with *“responsibility for the health of their peoples,”* and also noted that *“the achievement of any State in the promotion and protection of health is of value to all”* (WHO, 2006).

In the 75 years since this declaration, biopharmaceutical innovation has come to play an increasingly central role in protecting health and treating disease. Inspired, in part, by the wartime success of penicillin and sulfa drugs, medicine increasingly turned to the discovery and development of novel pharmaceutical products as a means for treating and preventing disease and improving health. In a series of studies on the impact of novel pharmaceutical products on human health starting in the late 1980s, Frank Lichtenberg estimated that drugs approved between 1986 and 2000 accounted for an increase in longevity of 0.8 years by 2000 (Lichtenberg, 2005), and that drugs approved after 1990 had contributed to an increase in longevity of 1.27 years by 2009, representing 70% of the total increase in longevity over the same period (Lichtenberg, 2014a). His work has also suggested that pharmaceutical products improved population health, as measured by the number of work loss days, school loss days, and hospital admissions (Lichtenberg, 2014b), and improved “activities of daily living” among the elderly (Lichtenberg, 2012). Moreover, many pharmaceuticals were shown to be effective in reducing healthcare costs by preventing disease or obviating more expensive treatments or

hospitalizations (Neumann et al., 2000). By 2018, the increasing use of medicines had created a global market for pharmaceutical products of more than \$1.2 trillion annually (Aitken & Kleinrock, 2019). In the United States, prescription sales in 2018 totaled \$476.2 billion, representing 10% of total healthcare spending (Schumock et al., 2019).

Government and industry both have critical roles in pharmaceutical innovation. As will be described in more detail in Section 2, contemporary science policy in the United States largely operationalizes a linear model of innovation, in which basic science, or use inspired basic science, performed in academic institutions and funded by the government provides fundamental insights or inventions; which are then transferred to industry for practical, commercial applications. The archetype of this model is the American government's Advanced Research Projects Administration (ARPA, now DARPA), whose pioneering work in information technology, computing and communications played a critical role in spawning the technology industry (Azoulay et al., 2019; Hafner & Lyon, 1998; Lazonick, Mazzucato, & Tulum, 2013).

A similar model has been evident in drug discovery and development. Government-funded, basic research has been shown to play a foundational role in pharmaceutical development (Comroe & Dripps, 1978; Toole, 2012). Our previous work has shown that NIH funding contributed to research underlying every one of the 210 new drugs approved from 2010–2016, representing an investment of more than \$100 billion (2000–2016) (Cleary et al., 2018; Cleary & Ledley, 2020). That work also showed that more than 90% of this funding was related to research on the biology underlying novel pharmaceutical products, rather than the drugs themselves (Cleary et al., 2018).

Virtually all of the pharmaceutical products on the market today, however, were developed and commercialized by for-profit companies (Kinch et al., 2014). Biopharmaceutical companies

invest an average of more than a billion dollars in the development of each new, approved product (DiMasi, Grabowski, & Hansen, 2016; Wouters, McKee, & Luyten, 2020) and are responsible for the manufacture and marketing of these products after approval.

This work was undertaken in the context of existential threats to both the public and private sector funding for the basic biomedical research that enables drug discovery and development. The threat to public sector funding for basic science has been acutely evident in recurring proposals from the Executive Branch to cut the budgets of the National Institutes of Health (NIH), National Science Foundation (NSF), and science programs at other agencies (Mervis, 2020a). While Congress has consistently resisted recent attempts to reduce the NIH budget (Mervis, 2020b), there is a significant long-term trend towards reduced public investment in research and development throughout the OECD countries (Archibugi & Filippetti, 2018). Moreover, continued growth of non-discretionary spending in the coming decades will leave a smaller proportion of the federal budget available for discretionary spending, including biomedical research (Hourihan, 2018).

Private sector funding of early-stage basic or applied research by the pharmaceutical industry is also under threat from several factors. One is the increased financialization of the pharmaceutical industry and its focus on maximizing shareholder value, which has reduced corporate investment in institution learning (Lazonick et al., 2017; Lazonick, Mazzucato, & Tulum, 2013; Lazonick & Tulum, 2011; Montalban & Sakinç, 2011, 2013; Tulum & Lazonick, 2018). The impact of financialization has been exacerbated by the increasing cost of biopharmaceutical research and decreasing return on investment (Pammolli, Magazzini, & Riccaboni, 2011; Scannell, Blanckley, Boldon, & Warrington, 2012; Steedman & Taylor, 2020), which have made such investment in research less attractive to shareholders.

Industry investment in R&D is further threatened by potential policy initiatives designed to reduce drug prices (Padula, 2019; Sachs, 2019). The prices of pharmaceutical products have risen sharply in recent decades, and there is growing concern that drug prices now limit their availability to those who need these products (Deb & Curfman, 2020; Hernandez et al., 2020; Kesselheim, Avorn, & Sarpatwari, 2016; NAS, 2018). Moreover, many of the largest pharmaceutical companies are highly profitable. Our research has shown that from 2000–2018, 35 of the largest pharmaceutical companies had cumulative revenue of \$11.5 trillion and net income (earnings or profits) of \$1.9 trillion, and were significantly more profitable than other companies in the S&P 500 (Ledley et al., 2020). While policies might be developed that balance the affordability of drugs with sustained innovation, previous studies showed that the Clinton-era initiatives aimed at reducing drug prices were associated with lower R&D spending in the pharmaceutical industry during the years these policies were being considered (Abbott & Vernon, 2007; Giaccotto, Santerre, & Vernon, 2005; Golec, Hegde, & Vernon, 2010; Vernon, 2005).<sup>2</sup>

This research was undertaken in the context of government’s *“responsibility for the health of their peoples”* and its vested interest in sustained biopharmaceutical innovation as one means of providing the *“the highest attainable standard of health.”* To the extent that novel pharmaceutical products contribute to achieving a higher standard of health and represent public value, this work provides insights into the broader concept of government as an “investor of first resort” in value creation (Block & Keller, 2015; Hopkins & Lazonick, 2014; Lazonick, 2017;

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<sup>2</sup> The Congressional Budget Office provided preliminary analyses of the effects of H.R.3 on pharmaceutical innovation in letters dated October 11, 2019 (<https://www.cbo.gov/system/files/2019-10/hr3ltr.pdf>) and December 10, 2019 ([https://www.cbo.gov/system/files/2019-12/hr3\\_complete.pdf](https://www.cbo.gov/system/files/2019-12/hr3_complete.pdf)). These analyses variously estimate that H.R.3 could lead to 8–15 fewer drugs coming to market (October, 2019) or as much as 10% (December, 2019).

Lazonick & Mazzucato, 2013; Mazzucato, 2011, 2016; Mazzucato & Semieniuk, 2017) as well as the “risk-reward nexus” that results in an unequal distribution of risk and reward between the public and private sector (Lazonick & Mazzucato, 2013).

This has created a critical need for a greater understanding of the role played by government in the biopharmaceutical innovation process, how value is created and returned through this process, and how to maximize the health benefits of this work. Given the rapidly changing landscape of biopharmaceutical innovation and public concern about the affordability and availability of medicines, as well as the acute health and economic shocks associated with the COVID-19 pandemic, there is an opportunity to apply evidence-based policies that leverage the role of government to promote effective innovation and value creation now and in the future.

### ***Outline of this research***

Section 2, Background and Literature, begins with a brief description of the linear model of innovation, which has long provided a conceptual framework for the biopharmaceutical innovation ecosystem. This classical model, which posits a directional flow of innovation from basic research→applied research→development→products and services, underlies much of the research on biopharmaceutical innovation and strategy, the process of drug development and regulatory review by the U.S. Food and Drug Administration (FDA), and the design of the Bayh-Dole Act. We describe the meaning of “basic” and “applied” research in this model, the differentiated roles of the public and private sector, and amendments to the classical model, with particular recognition of the role played by “use-inspired” basic research. To aid understanding, we also provide a short overview of the process for drug discovery and development, and

regulatory classifications of novel drug products related to their innovativeness and approval path.

We also provide an overview of the Bayh-Dole Act, as well as its impact on the biopharmaceutical innovation ecosystem. A complete review of the extensive literature on the Bayh-Dole Act and its impact is beyond the scope of our analysis. Our overview focuses on several key issues. First, we discuss the policy goals underlying the design of the Bayh-Dole Act. Second, we discuss the process of technology transfer/licensing by academic institutions. Finally, we consider the role of patents in the mechanisms for value creation and capture established by the Bayh-Dole Act. Specifically, we ask whether the restriction of Bayh-Dole to patentable results of government-funded research limits its applicability to promoting public value creation.

Section 3, Research Results and Discussion, describes our research in several discrete stages. The first step involved identifying and characterizing the new drugs (New Molecular Entities [NMEs]) approved from 2010–2019. We describe 356 products approved during this decade, their characteristics, biological targets, applications, and measures of the innovativeness or importance. The second step involved performing literature searches in the PubMed database to identify published literature directly related to either these drugs or their biological targets. We then used the Technology Innovation Maturation Evaluation (TIME) model to estimate when these bodies of research passed the *established* point of research maturation. Previous work has shown that an *established* body of research on novel targets is requisite for efficient drug development. Third, we use the NIH RePORTER database to identify published research arising from NIH grants, the specific grants (Programs), fiscal years (Funding Years), and Project Costs contributing to this research, and the patents that arose from the research results. Fourth, we describe several proxy measures for the innovativeness or importance of the new drugs approved

over this decade including first-in-class designations, and designations for expedited review and approval. Fifth, we examine the patents identified in the FDA Orange Book as providing exclusive marketing rights for approved products, and ask how many of these patents arose from the NIH funding and research detailed in this report.

Section 4, Conclusions, provides a brief discussion of the potential implications of this research for understanding the biopharmaceutical innovation ecosystem and formulating evidence-based policy to achieve “the highest attainable standard of health” and maximize public value creation. We also discuss the limitations of our methods and analysis, as well as areas for future research.

We want to express our particular gratitude to the Institute for New Economic Thinking for its support of this work and to Dr. Thomas Ferguson and Dr. William Lazonick for encouraging us to consider the larger economic policy implications of our work. This Working Paper describes a core dataset and analysis of the new drugs approved during the decade 2010–2019 as well as the substantial public sector investments made by the NIH that enabled the discovery and development of these products. These data describe the current state-of-the-art for drug development, factors that contribute to the persistently long timelines and high failure rate of discovery and development, the scope of the public sector investment in this process, and factors that limit the public’s control over the products and the value created by these investments. The work has implications for accelerating the translation of scientific discoveries for public value and formulating policies to ensure that science is used to achieve “the highest attainable standard of health” in a way that is both efficient and equitable. None of these issues are addressed in sufficient detail in this Working Paper; each requires far deeper consideration of the relevant literature and more complete analysis in the future. We are acutely aware of these limitations,

and look forward to productive discussions with readers who may find our consideration of these inadequate and identify areas for future investigation.



## Background and Literature

### *The linear model of biopharmaceutical innovation and role of the NIH*

The process of discovering and developing new medicines is classically described in terms of a linear model of innovation. In its simplest form, the model posits that there is a directional, “linear” flow of progress towards innovation from basic science, through applied science, and finally to the development and commercialization of novel products and services (Balconi, Brusoni, & Orsenigo, 2010; Edgerton, 2004; Godin, 2006). The linear model posits that there is a clear distinction between “basic” research, “applied” research, and development. “Basic research” is defined by the National Science Foundation (NSF) as being “...*undertaken primarily to acquire new knowledge of the underlying foundations of phenomena and observable facts, without any particular application or use in view,*” and is distinct from applied research, defined as being “...*directed primarily towards a specific, practical aim or objective.*” The penultimate step is development, defined as being “...*directed to producing new products or processes or to improving existing products or processes*” (NSF, 2018), which leads to commercialization. The concept of “basic science” has been extended by recognizing the role of “use-inspired basic research”, which is undertaken without specific products or processes in mind, but with the purpose of advancing economic gains or the public good (Stokes, 2011).

In biomedical research, the term “translational research,” is also used, which pertains to “...*applying discoveries generated during research in the laboratory, and in preclinical studies, to the development of trials and studies in humans*” (NIH, 2007). Translational research is most commonly undertaken in conjunction with assessing the safety and efficacy of specific medical products or interventions.

The linear model of innovation has been subject to intense analysis and criticism (Balconi et al., 2010; Godin, 2006). Nevertheless, the model had a central role in US science policies and an important imprint on the process of pharmaceutical development.

The influence of the linear model on US science policy dates from the work of Vannevar Bush and his 1945 report titled *The Endless Frontier* (Bush, 1945; Godin, 2006). This report recognized that the war effort had created “*a unique experiment of team-work and cooperation in coordinating scientific research and in applying existing scientific knowledge to the solution of the technical problems*” that could also be applied to the public welfare including the “*war of science against disease.*” Bush noted: “*Penicillin reached our troops in time to save countless lives because the Government coordinated and supported the program of research and development on the drug. The development moved from the early laboratory stage to large scale production and use in a fraction of the time it would have taken without such leadership.*”

Bush’s model for US science policy created a sharp distinction between basic and applied science, familiar to the linear model of innovation. He defined basic science as being “*...performed without thought of practical ends....*,” presaging language that would become embedded in the NSF definitions.<sup>3</sup> His science policy was predicated on the expectation that: “*Basic research leads to new knowledge. It provides scientific capital. It creates the fund from which the practical applications of knowledge must be drawn.*” He then anticipates that “*Industry*

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<sup>3</sup> “Basic research is performed without thought of practical ends. It results in general knowledge and an understanding of nature and its laws. This general knowledge provides the means of answering a large number of important practical problems, though it may not give a complete specific answer to any one of them. The function of applied research is to provide such complete answers. The scientist doing basic research may not be at all interested in the practical applications of his work, yet the further progress of industrial development would eventually stagnate if basic scientific research were long neglected.” (Bush, 1945)

*will fully rise to the challenge of applying new knowledge to new products. The commercial incentive can be relied upon for that” (Bush, 1945).*

He goes on to localize the basic research enterprise outside of industry, writing: *“Publicly and privately supported colleges and universities and the endowed research institutes must furnish both the new scientific knowledge and the trained research workers. These institutions are uniquely qualified by tradition and by their special characteristics to carry on basic research.”*

In contrast, he writes *“Industry is generally inhibited by preconceived goals, by its own clearly defined standards, and by the constant pressure of commercial necessity. Satisfactory progress in basic science seldom occurs under conditions prevailing in the normal industrial laboratory.”*

Recognizing the distinct enterprises involved in basic and applied research, Bush recommended that *“...basic research should be strengthened by use of public funds”* provided to colleges, universities and research institutes, and that the government should *“devise and promote the use of methods of improving the transition between research and its practical application in industry”* (Bush, 1945).

Three decades later, this model of medical innovation would be evidenced in the design of the “War on Cancer.” The 1971 act called for investments primarily in basic science related to mechanisms of normal and abnormal cell growth and differentiation based on *“the assumption that unbiased fundamental research would hold the key to unlocking the secrets of cancer”* (Haber, Gray, & Baselga, 2011). While it would be thirty to forty years before this research was sufficiently mature to generate effective cancer therapies (McNamee & Ledley, 2017), the large number of anticancer drugs approved in recent years can be directly traced to basic research originated during that period (Cleary & Ledley, 2020; McNamee & Ledley, 2017).

The linear model of innovation is deeply entrenched in the process of contemporary, targeted drug discovery and development. A typical schematic of the “targeted” drug discovery process is shown in Figure 1. In this model, drug discovery is enabled by a body of basic biomedical research that describes essential mechanisms of human biology and disease. This basic research delineates specific pathways for both disease and healing, and identifies the proteins that carry out essential functions on these pathways. This research also suggests strategies by which a chemical drug or manufactured protein might be targeted to a specific protein, and by attaching itself to this target, disrupt the disease process or promote healing.<sup>4</sup>

This information is then utilized in applied, or translational, research to identify or design drugs

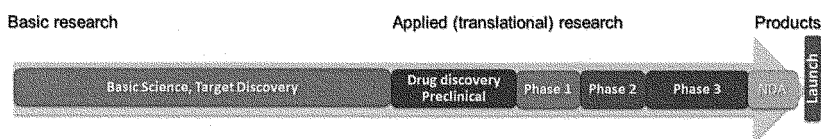


Figure 1. Schematic of drug discovery and development process.

that interact with the target protein in order to achieve these effects and are safe for use in humans, assess whether these drugs are effective and safe in laboratory or animal models, and develop methods for saleable production and quality control of these products. Only when this preclinical research meets the standards established by regulatory agencies, such as the Food and Drug Administration (FDA) in the US or European Medicines Agency (EMA) in the EU, can the first clinical studies be performed in human subjects.

<sup>4</sup> “Targeted” drug discovery is contrasted with “phenotypic” drug discovery, which involves isolating compounds from extracts of plants or microorganisms with known biological activities. “Phenotypic” compounds, or chemical modifications of these compounds, can enter development without prior knowledge of the biological target or mechanism of action.

Clinical trials proceed in defined phases. Phase 1 trials are classically undertaken in a small number of healthy volunteers to assess the safety of escalating doses of the drug. If the drug is shown to have a reasonable safety margin, the product will enter into Phase 2 trials in larger numbers of patients for an initial assessment of the product's effectiveness and effective dose. Only when a suitable dose and clinical application are identified, do products enter into "pivotal" Phase 3 trials designed to rigorously establish the safety and effectiveness of the product compared to an established therapy or placebo. If Phase 3 trials demonstrate significant effects, application can be made to regulatory agency for marketing approval. Following approval, the regulatory agencies can request Phase 4 studies to confirm key findings related to efficacy or safety.

In the United States, basic biomedical research is funded primarily by the NIH (Collins et al., 2016; Moses et al., 2015), whose stated mission is "*to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability*" ([www.nih.gov/about-nih/what-we-do/mission-goals](http://www.nih.gov/about-nih/what-we-do/mission-goals)). While the NIH allocates half of its research budget to "basic" science (Lauer, 2016), this research is essentially use-inspired, and undertaken with the expectation of bettering human health.

The NIH commitment to basic science is shaped by many competing priorities. Research funding from the NIH is not awarded by a central mechanism, but rather by individual Institutes, most of which have disease or demographic-specific missions. Moreover, the distribution of NIH funding is sometimes measured against the relative burden of disease in society to assess how closely its work is aligned with public needs (Gillum et al., 2011; Gross, Anderson, & Powe, 1999). Thus, NIH research funding is implicitly tied to use-inspired fields of study. The NIH is

also subject to congressional mandates for research earmarked to specific diseases or conditions, which requires funding to be explicitly linked to legislated goals (Sampat, 2012). It is worth noting that the NIH also supports applied biomedical research, clinical research, as well as research on medical and surgical practice.

The NIH awards grants to small businesses through Small Business Innovation Research (SBIR) mechanisms, which are designed to bridge the gap between basic research performed in academic settings, and the proof of principle experiments often required for commercialization (NRC, 2009). The NIH will also selectively conduct clinical trials with significant public health implications. In addition, the NIH has traditionally championed bench-to-bedside clinical research, though this role has declined significantly in recent decades (Nathan & Nathan, 2016; Nathan & Wilson, 2003). In recent years, there has been growing pressure on the NIH to participate in translational and applied research that is more directly related to clinical applications (Collins, 2011; Woodcock et al., 2014; Zerhouni, 2007), and work at the National Center for Advancing Translational Science (NCATS) is increasingly moving downstream to aid in drug discovery and preclinical analysis (Austin, 2018). There is also growing interest in the power of government-academic-industry partnerships to facilitate efficient translation of scientific advances into innovative products (Leydesdorff, 2000; Leydesdorff & Etzkowitz, 1998; Tralau-Stewart et al., 2009).

While government and academic institutions are showing increasing interest in applied and translational research, large pharmaceutical companies have become progressively disengaged from direct involvement in basic research. Large pharmaceutical companies increasingly focus on late-stage development, manufacture, and product marketing, and are filling their product

pipelines through acquisition of mature technologies, early-stage products, and nascent biotechnology companies (Wang, Plump, & Ringel, 2015).

We would emphasize that the linear model of innovation does not fully capture the dynamic nature of the innovation ecosystem. For example, it does not account for the push and pull of new technological capabilities and market needs (Godin & Lane, 2013), the interactions that occur at the boundary between the academic and commercial sectors (Cockburn & Henderson, 1996), the contributions made to use-inspired basic research by scientists in the biotechnology and pharmaceutical industries (Chakravarthy et al., 2016; Reichert & Milne, 2002; Zycher, DiMasi, & Milne, 2010); or recent efforts to promote translational science in the public domain (Collins, 2011; Varmus, 2006; Woodcock et al., 2014). Nor does the linear model apply to the conception of the “entrepreneurial university” (Etzkowitz, 2016, 2017) or the notion of an integrated “triple helix” of government-university-industry involvement in innovation (Leydesdorff & Etzkowitz, 1998). Nevertheless, as our data will confirm, all of the new drugs approved by the FDA over the past decade were developed and commercialized by industry.

### ***Defining the contribution of the public sector to biopharmaceutical innovation***

While the linear progression of biomedical science from basic research to applications is deeply integrated into the culture and organization of innovative activities, the classic work of Comroe and Dripps (1978) was the first to systematically establish this association by identifying the scientific foundation of major advances in cardiovascular medicine. A different approach was taken by Toole (2012), who showed a statistical association between NIH-funded basic research and new drug launches, with a 1% increase in NIH research being associated with a 1.8% increase in new drugs.

Our research group has examined the relationship between the advance of research on the biological targets for new drugs and drug approvals using an analytical model of technology maturation—the Technology Innovation Maturation Evaluation (TIME) model (McNamee, Walsh, & Ledley, 2017). The TIME model is based on patterns of innovation observed in many other fields, ranging from earth-moving equipment to computing and communications technologies. Namely, that there is a characteristic pattern of technological maturation, which can be modeled as a series of S-curves (Christensen, 1992, 1997; Foster, 1982; McNamee & Ledley, 2012). It has also been observed that nascent or emerging technologies are rarely able to meet the needs of established markets, even though they embody disruptive potential and will eventually match, and displace established technologies in the market once they mature (Christensen, 1992, 1997). Without reviewing persistent controversies about the theories of disruption that arise from this observation, the essential observation that technology maturation is related to the ability of a technology to meet the requirements of the market is consistent with observations in systems engineering that technology readiness is a critical factor in product success (Clausing & Holmes, 2010). The General Accounting Office has written “...*no element is more important than having technology, advanced enough to meet requirements but also mature enough to be predictably managed, available at the start of the product development cycle. Maturing new technology before it is included on a product is perhaps the most important determinant of the success of the eventual product*” (GAO, 1999).

McNamee and Ledley (2012) explored the application of this principle to biopharmaceutical development, positing that the FDA standards for safety, efficacy, and quality constituted the requirements of the market, and that the maturation of the underlying biomedical science would be requisite for achieving these demands. Using the cumulative number of publications on a



biological target for a drug or class of molecular entity as a proxy for technological advance, McNamee et al. showed that the advance of these technologies

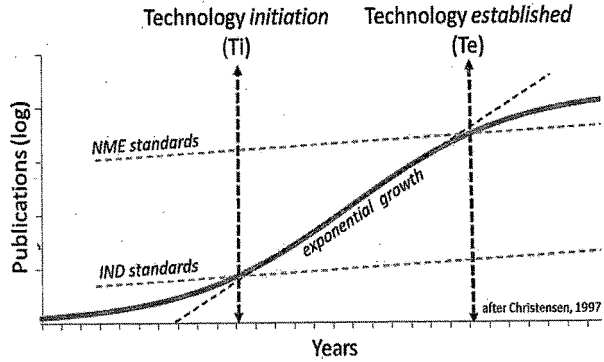


Figure 2. Schematic of basic research maturation and the TIME model.

followed a familiar S-curve pattern of maturation (McNamee & Ledley, 2017; McNamee, Walsh, & Ledley, 2017). The TIME model fits the cumulative number of publications on a specific research topic to an asymmetrical, exponentiated logistic function (Appendix A). Plotted on a log scale (Figure 2), this function exhibits the characteristic, logistic “S-curve” of technology maturation models observed in other fields (Christensen, 1992; Foster, 1982). The TIME model identifies two inflection points specifically related to basic biological research and drug development (Figure 2). The calculated *initiation* point, or point of maximum acceleration of publication activity, corresponds to the date of early discoveries that lead to exponential growth in research activity. In a series of papers, McNamee et al. also showed that the calculated *established* point, or point of maximum slowing of publication activity, corresponds to a maturation threshold, before which few targeted therapeutics are successfully developed (McNamee & Ledley, 2017; McNamee, Walsh, & Ledley, 2017). These studies also showed that the duration of clinical trials is longer when these trials begin before the established point, and that the first products resulting from the basic research are approved an average of 14 years after

this point (McNamee, Walsh & Ledley, 2017). These results are consistent with the expectation that a mature body of foundational research is requisite for the efficient discovery and development of targeted therapeutics. Specifically, it suggests that while initial scientific insights or inventions may be sufficient for scientific publications, patents, or filings of Investigational New Drug (IND) applications to begin clinical trials, they are rarely sufficient to meet the requirements for new drug approval. A series of follow-on studies have extended this concept, showing that the first approval of targeted cardiovascular drugs, targeted cancer drugs, gene therapies, and nucleotide therapies all followed the maturation of the underlying basic biomedical research (Beierlein, McNamee, & Ledley, 2017; Beierlein et al., 2017; Ledley et al., 2014; McNamee & Ledley, 2017; McNamee, Walsh, & Ledley, 2017).

Many studies, however, have shown a more limited impact of government-funded, academic research in products coming to market. Stevens et al. (2011) estimated that from 1990 to 2007 9.3% of new drugs, as measured by the number of New Drug Applications (NDAs), were first patented in public sector research institutions and transferred to industry. This fraction is similar to estimates by Kaitin et al. (1993) that 7.6% of drugs approved from 1981–1990 and 6.7% of new drugs approved from 1990–1999 (DiMasi, Hansen, & Grabowski, 2003) originated outside of industry (3.2% in government, academic/nonprofits 3.5%). Similarly, Sampat (2009) found that from 1988–2005, 7.7% of all NDAs and 10.3% of New Molecular Entities (NMEs) described in these NDAs, are based on university-owned patents cited in the FDA's Orange Book. Using a cohort approach, Nayak et al. described that 19% of 248 new drugs approved from 2008–2018 had their origin in publicly supported research and development (Nayak, Avorn, & Kesselheim, 2019).

Sampat and Lichtenberg (2011) examined the prior art referenced in patents for new drug approvals, finding that from 1988–2005, 47.8% of approvals were associated with a patent that cited prior art from the public sector (public sector patent or government publication), despite only 9% being directly associated with a public sector patent. These results are similar to those described by Patridge et al. (2015) who found that of the 1,453 drugs approved by the FDA through 2014, academic organizations were the first to publish the synthesis or purification of the compound for 801 (55%), but filed the investigational new drug (IND) status for only 21 (1.5%).

Case study methods generate similar results. Cockburn and Henderson (2000) examined the development of 21 drugs considered to have the most impact on practice from 1965–1992, finding that 76% were developed with some input from the public sector. Chakravarthy et al. (2016) examined the development of 19 of the “most transformative” drugs of the past 25 years, finding that, while only 15% of these drugs were discovered in the public sector, the public sector contributed to 54% of basic science milestones.

Our 2018 study by Cleary et al. looked explicitly at the contribution of NIH-funded basic science to new drugs approved from 2010–2016. That study identified more than 2 million research publications in the biomedical literature (PubMed) in this interval related to the 210 drugs approved or their 151 biological targets. Of these publications, more than 600,000 (29%) cited federal research support comprising more than 200,000 fiscal years of project funding (1985–2016) and more than \$100 billion in project costs since 2000. Significantly, NIH-funded research was identified in association with every new drug approved from 2010–2016.

Cleary et al. also demonstrated that more than 90% of the NIH-funded research was associated with basic science publications on the biological targets rather than the drugs. In contrast, less

than 10% of the NIH funding was associated with applied (or translational) science for these specific drugs (Cleary et al., 2018). All of these products were subsequently developed and commercialized by for-profit, biopharmaceutical companies.

In a follow-on study of the 59 new cancer drugs included in the original analysis, Cleary and Ledley (2020) noted that the total amount of NIH funding attributable to research on these drugs or their biological targets approached, or exceeded, the total budgets of the National Cancer Institute (NCI) and the NIH's own estimate of spending on cancer research in the Research Condition and Disease Categorization (RCDC) database. Their analysis showed that much of the foundational research for new cancer drugs was, in fact, funded by institutes with other disease-focused missions including the NIAID, NHLBI, and NIDDK. This suggested that “basic” research in areas such as immunology, funded by institutes focused on immune diseases such as allergy, blood diseases, or arthritis, contributed to the foundational research underlying new cancer therapies (Cleary & Ledley, 2020). Such “spillover” effects are the result of the government’s ability to invest in broad-based, basic research that is not restricted to specific product applications.

### ***The role of Bayh-Dole in realizing the public value of science***

Passage of the Bayh-Dole Act of 1980,<sup>5</sup> operationalized the “*transition between research and its practical application in industry*” anticipated by *The Endless Frontier* and the linear model of innovation. Bayh-Dole did this by authorizing public sector institutions and small businesses to patent and retain inventions made with federally-funded research, and allowing these institutions,

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<sup>5</sup> The Bayh-Dole Act is Public Law 96-517, titled the Patent and Trademark Law Amendments Act, and is codified in 35 U.S.C. 200-212 and 37 CFR 401. <https://grants.nih.gov/grants/bayh-dole.htm>

as well as the government, to enter into exclusive license agreements with private sector companies for development and commercialization, subject to a patent rights clause (NRC, 2011; Sampat, 2009; Stevens, 2004). Over the past forty years, Bayh-Dole has become a much practiced, criticized, and imitated keystone of the innovation ecosystem, particularly for biopharmaceutical products (Loise & Stevens, 2010; Mowery & Sampat, 2004; NRC, 2011; Stevens, 2004).

Prior to Bayh-Dole, inventions/discoveries made under federally-funded research were formally the property of the government. Prior to the 1960s, government was not the major source of funding for academic research, and more than 75% of Carnegie research universities entrusted the patenting and licensing of university research to an independent entity, the Research Corporation (Sampat, 2009). As government funding for academic research grew through the 1960s and 1970s, it was recognized that advances were being made that were patentable and of interest to industry, and systems were developed for universities to individually enter into Institutional Patent Agreements (IPA) with the government (Mowery & Sampat 2004). Each government agency was empowered to develop its own patent policies consistent with their distinct missions, which led to wide variation in the terms of IPAs between different agencies and institutions (Sampat, 2009). Moreover, the government commonly granted only non-exclusive licenses, which often did not align with the interests of industry (Loise & Stevens, 2010). In 1976, the Federal Council for Science and Technology estimated that only 5% of the 28,000 patents owned by the federal government had been licensed (FCST, 1968; Sampat, 2006) at a time when policy makers were searching for ways to stimulate the American economy (Stevens, 2004). This was recognized to be an inefficiency that could be preventing American industry, and consequently taxpayers, from capitalizing on groundbreaking research.

Bayh-Dole created a uniform policy allowing institutions receiving federal research funding to patent the results of this research and issue exclusive licenses. Institutions were expected to have agreements with their faculties and staff that required the disclosure of federally-funded inventions to the university and assignment of their rights to the institution. Institutions then had the option of patenting the invention at their own expense, or returning the rights to the inventors or licensing the resulting patents to industry for development. The federal government retains a “nonexclusive, nontransferable, paid-up license” to the invention as well as “march-in rights.” March-in rights give the government the ability to grant itself a license to the invention when the institution or its licensee does not take “effective steps” to practice the invention or in response to health, safety, or other “public use specified by federal regulations” that are “not reasonably satisfied” by the institution or licensee without direct government oversight (CFR, 2010; Thomas, 2016; Treasure, 2016). Patents resulting from government-funded research are also required to have a “government-interest” disclosure outlining the governments rights to that patent, and these patents are subject to various reporting requirements. Institutions were expected to have agreements with their faculties and staff that assigned the rights to government-funded inventions to the institution, and many set up technology transfer or licensing offices dedicated to the productive management of this intellectual property.

Implicit in the Bayh-Dole Act was the assumption that taxpayers would benefit from industrial development of licensed technologies in terms of the products, jobs, and economic growth that would result, that non-profit institutions would invest the proceeds from technology licensing in the public interest consistent with their charters, and that the growth of small businesses, which were considered to be the wellspring of innovation and economic growth, would be promoted.

As a practical matter, patents are central to the structure of the Bayh-Dole Act and, thus, the assignment and licensing of the intellectual property rights resulting from government-funded research governed by that Act.<sup>6</sup> For the results of a research project to be patentable, they must meet five criteria: (1) describe patentable subject matter; (2) utility; (3) novelty; (4) non-obviousness; and (5) enablement.

Not all research, however, is designed to meet these standards. Specifically, patent law requires the inventor to recognize a functional purpose or usefulness of the invention, and also provide sufficient information to enable those “*skilled in the art to reduce it to practice without the exercise of extensive experimentation or the exercise of inventive skill.*” As such, pure “basic” research that undertaken “*without any particular application or use in view*” implicitly may not meet the utility requirement. Moreover, given the complexity of translating biological discoveries into clinical applications (Collins, 2011), such discoveries often require “extensive experimentation” and “inventive skill” and may not satisfy the standards of enablement.

Li, Azoulay, and Sampat have demonstrated that only 8.4% of NIH grants generate a patent directly, but that 31% generate results that are cited as “prior art” in subsequent grant applications. They conclude that the greatest impact of NIH funding is not captured directly by patents, but rather indirectly by creating “art” that leads to the invention (without making it obvious) or enables the invention to be practiced (Li, Azoulay, & Sampat, 2017). They also

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<sup>6</sup> Other forms of intellectual property arising from basic research may include trade secrets and know-how (an intangible, intellectual property right). These are defined as: *Trade Secrets*: “Information, including a formula, pattern, compilation, program, device, method, technique, or process that: (i) Derives independent economic value, actual or potential, from not being generally known to, and not being readily ascertainable by proper means by, other persons who can obtain economic value from its disclosure or use; and (ii) Is the subject of efforts that are reasonable under the circumstances to maintain its secrecy” ([https://www.law.cornell.edu/wex/trade\\_secret](https://www.law.cornell.edu/wex/trade_secret)); and *Know-how*: “The ability to achieve a practical end due to knowledge and/or skill” (<https://www.law.cornell.edu/wex/know-how>).

found that less than 1% of NIH grants are directly acknowledged by a patent associated with a marketed drug in the FDA Orange Book,<sup>7</sup> but 5% of grants result in publications that represent art for drug patents.

Their work also assessed the “basicness” of the NIH-funded research using a rubric with four criteria: *“whether the research is disease-oriented, whether it is focused on patients, and whether it is solicited by the funder or is investigator-initiated; for the subset of grants that are not disease-oriented”* (Li et al., 2017). Using this rubric of “basicness,” the authors observed no association between the “basicness” of research and the likelihood of being cited by a patent. More recently, Long (2019) examined the government contribution to Orange Book patents associated with 300 top-selling drugs from 2013–2017, finding that only 2.6% of patents included a “government-interest” statement, and that 8.6% of drugs had at least one patent with a “government-interest” statement.

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<sup>7</sup> The FDA publishes a list of approved drug products known as the Orange Book in accordance with the Hatch-Waxman Amendments (1984). The Orange Book *“identifies products that have qualified under the FD&C Act for periods of exclusivity and provides patent information concerning the approved drug products”* (<https://www.fda.gov/drugs/development-approval-process-drugs/orange-book-preface>). The patents listed in the Orange Book represent only those identified by the FDA as being related to the market exclusivity of the product and is not representative of all patents related to the discovery or development of the drug. Patents are only listed in the Orange Book as long as they provide marketing exclusivity, and are eliminated from the database after patent term expiration or successful legal challenge. The complete historical record of patents was obtained from DrugPatentWatch (<https://www.drugpatentwatch.com/>) and data through 2016 was obtained from Dr. Heidi Williams (<http://data.nber.org/fda/orange-book/historical/1986-2016/>).



## 2. Research Results and Discussion

### *Drugs approved by the FDA 2010–2019*

We identified new drugs approved by the FDA from 2010 through 2019 by the Center for Drug

Evaluation and Research

(CDER) or the Center for

Biologics Evaluation and

Research (CBER)<sup>8</sup> (Figure

3). This study excluded

diagnostic products,

products derived from blood

or tissue, and vaccines.

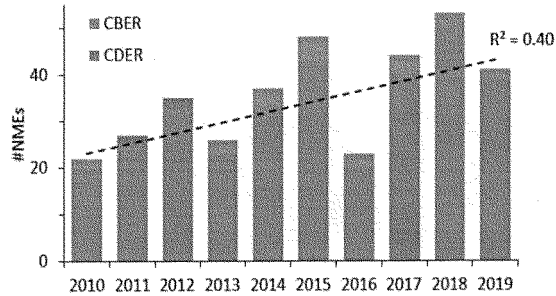


Figure 3. Annual FDA approvals, 2010–2019.

A total of 356 new drugs termed NMEs were approved from 2010–2019, of which 331 were

approved by CDER and 25 approved by CBER over this interval (Table 1). Despite year-to-year

variation,<sup>9</sup> there was a significant increase in approvals over the 10-year period (Chi-squared,

<sup>8</sup> The FDA approves drugs through two statutory mechanisms. The Center for Drug Evaluation and Research is authorized by the Federal Food, Drug, and Cosmetic Act, and regulates small molecules and many recombinant, biological products that can be well-characterized. The Center for Biologics Evaluation and Research is authorized under the Public Health Service Act, while also subject to the Federal Food, Drug and Cosmetic Act, and regulates biological and blood products defined by their manufacture. New drug classes regulated by CBER include gene therapies, cell and tissue products, vaccines, products for xenotransplantation, and vaccines.

<sup>9</sup> The FDA accounted for the low number of approvals in 2016 as an anomaly resulting from the early, expedited approvals of five drugs in 2015 that originally had PDUFA dates in 2016 (FDA, 2016 Novel Drugs Summary January 2017) ([www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DrugInnovation/UCM536693.pdf](http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DrugInnovation/UCM536693.pdf)). The Prescription Drug User Fee Amendments (PDUFA) authorizes the FDA to collect user fees from pharmaceutical companies in exchange for a determined timeline for reviewing applications for drug approval (<https://www.fda.gov/industry/fda-user-fee-programs/prescription-drug-user-fee-amendments>).

**Table 1. Product class and FDA expedited drug status of New Molecular Entities (NMEs) approved by the FDA from 2010–2019**

|                                                 |                      | Total NME | CDER <sup>1</sup> | CBER <sup>2</sup> |
|-------------------------------------------------|----------------------|-----------|-------------------|-------------------|
|                                                 | All                  | 356       | 331               | 25                |
| <b>Product class</b>                            |                      |           |                   |                   |
|                                                 | Phenotypic           | 91        | 91                | n/a <sup>3</sup>  |
|                                                 | Targeted             | 265       | 240               | 25                |
|                                                 | Biologic             | 126       | 101               | 25                |
|                                                 | NCE                  | 230       | 230               | n/a <sup>4</sup>  |
|                                                 | First-in-class       | 136       | 136               | n/a               |
|                                                 | Orphan drug          | 151       | 146               | 5                 |
| <b>Expedited designation (CDER)<sup>5</sup></b> |                      |           |                   |                   |
|                                                 | Accelerated approval | 46        | 46                | n/a               |
|                                                 | Breakthrough therapy | 73        | 73                | n/a               |
|                                                 | Fast track           | 123       | 123               | n/a               |
|                                                 | Priority             | 181       | 181               | n/a               |

(1) Center for Drug Evaluation and Research (CDER); (2) Center for Biologics Evaluation and Research; (3) All biological products are treated as "targeted" therapeutics; (4) All New Chemical Entities (NCEs) are regulated by CDER; (5) Expedited tracks for approval are only available through CDER. n/a - not applicable

$p < 0.0001$ ) (Figure 3). New drugs were classified as New Chemical Entities (NCEs) or biological products.

An NCE is a drug product comprising a small molecule that can be produced by chemical synthesis. These products are regulated by CDER and represent the majority of all drug products.

A biologic is a drug product comprising a complex molecular structure or cell, typically manufactured by production in a living system such as an animal, plant cell, or microorganism.

Biologics can be regulated by either CDER or CBER.

Drug approvals were also categorized by their method of discovery as either phenotypic or targeted (Table 1). Targeted discovery begins with characterizing the structure and function of a biological molecule, usually a protein, with known functions in disease or health, and then

developing a molecular entity that attaches to that target and alters its function. Our definition of targeted therapeutics also includes recombinant copies or analogs of naturally occurring biological proteins as well as monoclonal antibodies (mAbs) against a specific biological protein. Of the 356 NMEs, 265 (74%) were classified as targeted.

In contrast, phenotypic discovery begins with an observation of biological changes in living systems, commonly plants or microorganisms, and the subsequent isolation of the molecular entities involved in that change. Such approaches do not rely on knowledge about the structure or function of any specific drug target or its role in disease (Moffat et al., 2017). Of the 356 NMEs, 91 (26%) were classified as phenotypic.

The therapeutic area for each product was determined from the FDA labeled indication and the Anatomical Therapeutic Chemical (ATC) Classification System (Nahler, 2009) and shown for both the 2010–2016 dataset (Cleary et al., 2018) and products approved 2017–19 (Figure 4).

Antineoplastic drugs constituted the greatest fraction of approvals (29%) for the full decade, followed by central nervous system (CNS) and cardiovascular.

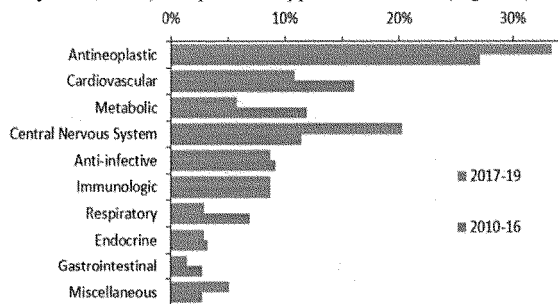


Figure 4. Percentage of NMEs in different therapeutic areas approved from 2010–2016 or 2017–2019.

The relative number of products varied from 2010–2016 and 2017–2019, with cardiovascular being the second most prevalent therapeutic class from 2010–2016 followed by metabolic, but the fraction of both dropping commensurate with increases in CNS after 2017.

We identified the start date for each phase of clinical development from PharmaProjects or Clinicaltrials.gov. We then calculated the time from the initiation of each clinical trial phase to first product approval (Figure 5). Data were obtained for 188 products entering Phase 1, 256 products entering Phase 2, and 348 products entering Phase 3.<sup>10</sup> The median length of time from Phase 1 to approval was 8 years, the median length of time from Phase 2 to approval was 7 years, and the median length of time from Phase 3 to approval was 4 years. These values are consistent with the

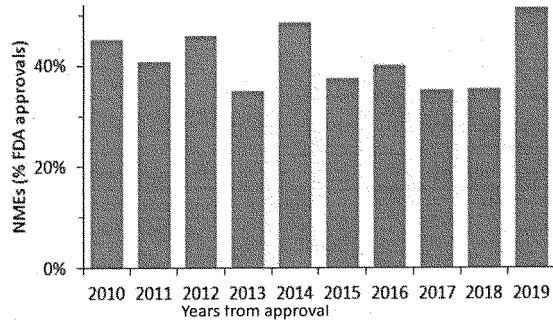


Figure 5. Percentage of NMEs categorized as first-in-class, 2010–2019.

lengths of clinical trials reported by others (DiMasi et al., 2016; Martin, Hutchens, & Hawkins, 2017; McNamee, Walsh, & Ledley, 2017; Wong, Siah, & Lo, 2019).

### *Measures of innovativeness*

There are no generally accepted metrics for judging the innovativeness or importance of novel biopharmaceutical products (Kesselheim et al., 2015). To assess innovativeness, products were classified by several different indicators including whether the product was categorized as first-

<sup>10</sup> The PharmaProjects database is restricted to publicly available information on the start of clinical trials. Phase 1 and Phase 2 trials in large companies are often not considered material, and are not publicly reported. In 2007, the FDA Amendments Act (FAAA801 (<https://www.govinfo.gov/content/pkg/PLAW-110publ85/pdf/PLAW-110publ85.pdf#page=82>)) created a statutory requirement for reporting information on clinical trials to a “clinical trial registry data bank,” ClinicalTrials.gov (<https://clinicaltrials.gov/ct2/manage-recs/fdaaa>). Compliance with this requirement remains incomplete (DeVito, Bacon, & Goldacre, 2020). This study used only Phase 1 and Phase 2 dates available from PharmaProjects, but identified Phase 3 start dates missing from PharmaProjects in ClinicalTrials.gov. Drugs without Phase 3 start dates in either database were confirmed to have been approved after a pivotal Phase 2 trial.

in-class and whether it was designated for expedited review. First-in-class drugs were categorized using the method of Lanthier et al. (Lanthier et al., 2013; Miller & Lanthier, 2015) as reported in CDER annual reviews of new drug approvals. CBER does not provide this categorization. This method categorizes a new drug as first-in-class if it is “pharmacologically innovative because each represents a new pathway for treating a disease.” This categorization explicitly includes the first drug approval related to a novel biological target, and can also include certain novel mechanisms of action on that target. For example, drugs that are selective agonists (stimulators), antagonists (inhibitors) or that bind to a different physical region on the target protein may all be considered first-in-class drugs for that target. This categorization excludes products that may offer major advances in treatment over products using the same pathway, termed “advance-in-class,” as well as products that represent an addition-to-class, even though such products may reduce cost, reduce adverse events, improved dosing (compliance), or uniquely benefit subsets of patients. Of the 331 new drugs in our study approved by CDER from 2010–2019, 136 (41%) were categorized as first-in-class. The percentage of first-in-class drugs varied from 35–51% with no significant trend through the decade (Figure 6). The fraction of first-in-class drugs in this decade was similar to historical averages, and was higher than the late 1990s and early 2000s, when the apparent paucity of first-in-class drugs attracted considerable attention (Grabowski & Wang, 2006; Lanthier et al., 2013).

CDER has four expedited approval tracks<sup>11</sup> termed Fast Track, Breakthrough Therapy, Accelerated Approval, and Priority Review, each intended to accelerate the development and review process for drugs deemed to treat serious diseases (Darrow, Avorn, & Kesselheim, 2020; Hwang, Darrow, & Kesselheim, 2017; Kesselheim et al., 2015). Both CDER and CBER products can also be designated as Orphan Products.

Of the 331 CDER approvals from 2010–19, 46 (14%) were designated for Accelerated Approval, 73 (22%) as Breakthrough Therapies, 123 (37%) as Fast Track, and 181 (55%) for Priority Review (Table 1). Overall, 198 drugs (76%) had at least 1 expedited designation, with an average of 1.28 designations per drug over the 10-year period (Table 3). Both the number of products and percentage of annual approvals having at least one expedited designation increased significantly over the decade (Figure 7A) as did the average number of expedited designations per approval (Figure 7B). These totals and trends are consistent with those described by others (Hwang et al., 2017; Kesselheim et al., 2015; Vadola et al., 2017). Orphan drug designation is granted to products designed to treat a rare disease or condition, or a subset of a disease or condition, affecting less than 200,000 people in the United States<sup>12</sup> (Boat & Field, 2011). The designation provides for treatment use of investigational drugs, a facilitated approval process, tax credits, and an extended period of exclusivity and applies to both CBER and CDER products.

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<sup>11</sup> Expedited approval tracks (definitions quoted from: <https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review>): *Fast track* - a process designed to facilitate the development, and expedite the review of drugs to treat serious conditions and fill an unmet medical need; *Breakthrough Therapy* - a process designed to expedite the development and review of drugs which may demonstrate substantial improvement over available therapy; *Accelerated Approval* - these regulations allowed drugs for serious conditions that filled an unmet medical need to be approved based on a surrogate endpoint; *Priority Review* - Priority Review designation means FDA's goal is to take action on an application within 6 months.

<sup>12</sup> The Orphan Drug Designation is described in CFR Title 21 PART 316 [https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=&SID=718f6fcbc20f2755bd1f5a980eb5cecd&mc=true&n=sp21.5.316.c&r=SUBPART&ty=HTML#se21.5.316\\_120](https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=&SID=718f6fcbc20f2755bd1f5a980eb5cecd&mc=true&n=sp21.5.316.c&r=SUBPART&ty=HTML#se21.5.316_120).

From 2010–19 approval period, 146 (44%) of CDER approvals were granted orphan status and 5 (25%) for CBER.

The significance of expedited designations as a proxy for innovativeness is unclear. Drugs receiving at least one expedited designation have been reported to provide greater health benefits than other products (Chambers et al., 2017). There is growing concern, however, that the reduced clinical trials may lead to product approvals on the basis of incomplete results that are not confirmed by more robust, follow-on studies (Darrow, Avorn, & Kesselheim, 2014), that the

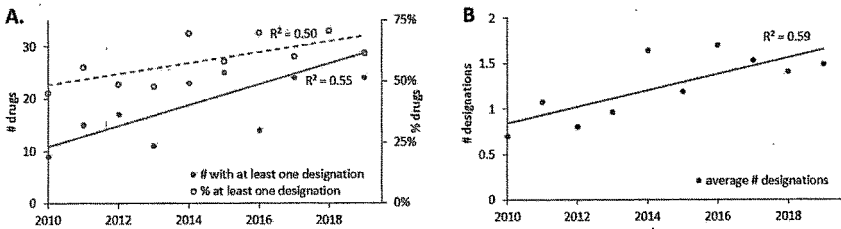


**Figure 7. Expedited approval designations for new drugs approved 2010–2019.** A. Drugs with at least one expedited approval designation. B. Average number of expedited approval designations.

clinical impact of products approved on the basis of surrogate end points may prove to have only limited clinical impact (Gyawali, Hey, & Kesselheim, 2019); that data on drug safety may not be complete (Mostaghim, Gagne, & Kesselheim, 2017); or that confirmatory trials may not be completed or are completed only years after the products are on the market (Beaver et al., 2018; Naci, Smalley, & Kesselheim, 2017; Woloshin et al., 2017).

### ***Modeling technology maturation***

As described briefly in Section 1, Introduction, the TIME model assesses the maturation of biomedical research on specific topics and the readiness of this technology to support successful drug development. Specifically, it calculates a point of technology *initiation* ( $T_i$ ), which is

commonly associated with a seminal insight or invention that gives rise to a new area of inquiry, and a point the technology is *established* (Te), which previous studies have shown generally precedes first approval of a new drug based on that research (Figure 2).

We modeled the maturation of research on the biological targets of new drugs approved from 2010–2019. For each new drug, or NME, the biological target was identified from the FDA label and confirmed from PharmaProjects or literature review. For “targeted” therapeutics, the target was the protein or its function used to discover the new drug. For “phenotypic” therapeutics, the target was the protein or its function most commonly associated with the drug’s activity. For biologics other than monoclonal antibodies, the biological target was the entity comprising, or analogous to, the NME. For example, for insulin analogs, insulin is treated as the “target.” We then searched PubMed (Medline)<sup>13</sup> using the updated Automatic Term Mapping (May 2020) with Boolean search terms optimized for specificity and breadth by examining publication titles, abstracts, and descriptions of search results for randomly selected result pages and eliminating query terms that introduced irrelevant results. Publications were identified by a PubMed Identifier (PMID) and publication year and all data collected using web data mining in the R programming language.

A total of 219 unique biological targets were identified, associated with 337 drugs. The remaining 19 NMEs could not be associated with a discrete biological target or the target is unknown. Of the 219 targets, research on 159 (73%) exhibited an exponentiated logistic pattern of technology advance and reasonable fit with the TIME model (exponentiated logistic function). Predictable exceptions included technologies that exhibited an exponential pattern of growth,

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<sup>13</sup> PubMed: <https://pubmed.ncbi.nlm.nih.gov/>, accessed May 12, 2020.



consistent with an immature technology, and technologies exhibiting complex, multiphasic S-curves, consistent with the observation of technological maturation by successive S-curves (Christensen, 1997; Foster, 1982). Some did not exhibit an exponential growth phase. The 159 technologies successfully modeled were associated with 232 product approvals.

Figure 8 shows the time intervals from Ti and Te to first approval for new drugs approved 2010–2019 for which data were available. Table 2 shows the median intervals from Ti, Te, Phase 1 start, Phase 2 start, and Phase 3 start for products approved 2010–2019 and different subsets of these products.

The median interval from Ti to approval was 44 years, representing the interval from an initiating event that created a period of exponential growth of research related to the target, to approval of a drug associated

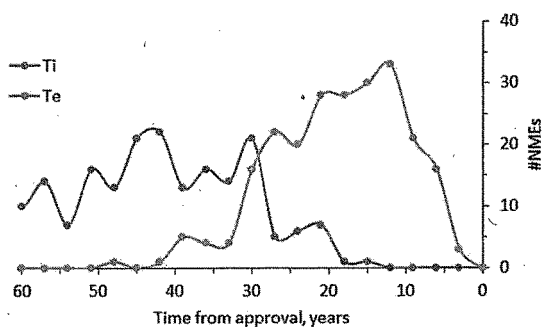


Figure 8. Time from technology *initiation* (Ti) or technology *established* (Te) points to first approval, 2010–2019.

with that target. This initiating event often does not involve the actual discovery or characterization of the target, but rather research on the targets or

Table 2. Years from R&amp;D milestones to approval for NMEs approved 2010–2019.

| Subset of drugs approved<br>2010–2019   | Initiation point<br>(Ti) |                 |     | Established point<br>(Te) |     |                 | Phase 1 |                 | Phase 2 |                 | Phase 3 |                 |
|-----------------------------------------|--------------------------|-----------------|-----|---------------------------|-----|-----------------|---------|-----------------|---------|-----------------|---------|-----------------|
|                                         | N                        | Median<br>(yrs) | N   | Median<br>(yrs)           | N   | Median<br>(yrs) | N       | Median<br>(yrs) | N       | Median<br>(yrs) | N       | Median<br>(yrs) |
|                                         |                          |                 |     |                           |     |                 |         |                 |         |                 |         |                 |
| All                                     | 232                      | 44              | 232 | 17                        | 117 | 9               | 170     | 7               | 226     | 4               |         |                 |
| <b>Drug subset</b>                      |                          |                 |     |                           |     |                 |         |                 |         |                 |         |                 |
| CDER                                    | 227                      | 44              | 227 | 17                        | 114 | 9               | 168     | 7               | 221     | 4               |         |                 |
| CBER                                    | 5                        | 47              | 5   | 25                        | 3   | 7               | 2       | 8               | 5       | 5               |         |                 |
| Phenotypic                              | 60                       | 58**            | 60  | 19                        | 30  | 10              | 43      | 7               | 60      | 5               |         |                 |
| Targeted                                | 172                      | 43              | 172 | 17                        | 87  | 9               | 127     | 7               | 166     | 4               |         |                 |
| NCE                                     | 161                      | 44              | 161 | 17                        | 73  | 9               | 113     | 7               | 158     | 4               |         |                 |
| Biologic                                | 71                       | 43              | 71  | 19                        | 44  | 9               | 57      | 7               | 68      | 5               |         |                 |
| First-in-class                          | 97                       | 44              | 97  | 17                        | 58  | 9               | 80      | 7.5             | 93      | 4               |         |                 |
| Follow-on                               | 129                      | 43              | 129 | 17                        | 56  | 9               | 88      | 7               | 127     | 4               |         |                 |
| Orphan                                  | 91                       | 47              | 91  | 18                        | 57  | 9               | 71      | 7               | 86      | 4               |         |                 |
| Other                                   | 136                      | 42              | 136 | 15                        | 57  | 9               | 97      | 7               | 135     | 4               |         |                 |
| <b>Designation for expedited review</b> |                          |                 |     |                           |     |                 |         |                 |         |                 |         |                 |
| Accelerated approval                    | 24                       | 44              | 24  | 17                        | 16  | 7.5             | 23      | 6*              | 23      | 2***            |         |                 |
| other                                   | 203                      | 44              | 203 | 17                        | 98  | 9               | 145     | 8               | 198     | 4               |         |                 |
| Breakthrough therapy                    | 41                       | 46              | 41  | 18                        | 22  | 7.5             | 30      | 6               | 38      | 3***            |         |                 |
| other                                   | 172                      | 43              | 172 | 17                        | 86  | 9               | 129     | 7               | 169     | 5               |         |                 |
| Fast track                              | 71                       | 43              | 71  | 15                        | 39  | 8               | 52      | 7               | 69      | 3               |         |                 |
| other                                   | 156                      | 44              | 156 | 18                        | 75  | 9               | 116     | 7               | 152     | 5               |         |                 |
| Priority                                | 115                      | 45              | 115 | 17                        | 71  | 8               | 87      | 7*              | 110     | 3.5***          |         |                 |
| other                                   | 112                      | 43              | 112 | 17                        | 43  | 9               | 81      | 8               | 111     | 5               |         |                 |

Ti and Te data are shown for 232 of 356 drugs approved by the FDA from 2010 to 2019. Of the other drugs, 19 were phenotypic with no known target/mechanism of action, and 105 exhibited TIME model growth patterns that did not fit the exponentialized logistic model. Phase 1 and Phase 2 start dates shown are those given in PharmaProjects. Phase 3 start dates were from PharmaProjects or ClinicalTrials.gov. Statistical analysis compared associated subcategories, CDER vs. CBER, first-in-class vs. follow-on, phenotypic vs. targeted, NCE vs. biologic, and CDER designations vs. non-designated, using a Mann-Whitney, nonparametric, two independent samples test. With a Bonferroni correction of 9, a difference with a p value below 0.0056 was considered significant ( $p > 0.0056$ , \*  $p < 0.0056$ , \*\*  $p < 0.0011$ , \*\*\*  $p < 0.0001$ ).

technologies that led to that discovery (Beierlein, et al., 2017; McNamee, Walsh & Ledley, 2017). The median interval from Te to approval was 17 years, representing the time from maximum slowing of exponential advances on the drug target to successful approval of a drug based on these advances. Both values are commensurate with those described previously (McNamee, Walsh, & Ledley, 2017).

The clinical timelines from the initiation of the first Phase 1, Phase 2, or Phase 3 trials to approval is shown in Table 2. The median time from initiation of Phase 1 to approval was 9 years, from initiation of Phase 2 to approval was 7 years, and from initiation of Phase 3 to approval was 4 years. The significance of a mature foundation of basic research and drug approvals is evident in two observations. First, Figure 9A shows that drug approvals lag after the *established* point of the technology (Te) with a median of 17 years. Moreover, no new drugs in this study were approved before the *established* point and only 3 within the first three years after this point. This is consistent with previous observations showing that approval of targeted cardiovascular drugs (Beierlein et al., 2017), cancer drugs (McNamee & Ledley, 2017), and nucleotide therapeutics (Beierlein, McNamee, & Ledley, 2017) occurred uniformly after the

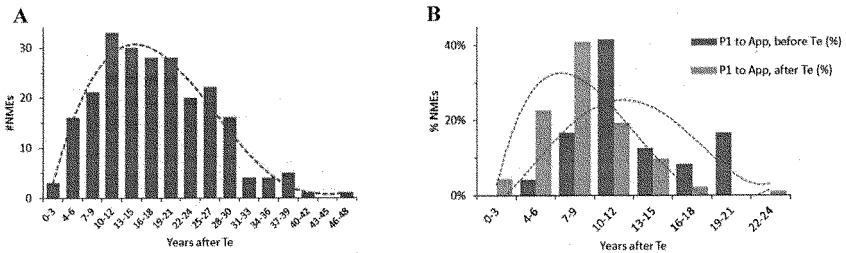


**Figure 9. Time of first NME approval after established point (Te) of research on the drug target.** A. Time after Te for all NMEs. B. Time after Te for NMEs beginning clinical trials before Te and those beginning clinical trials after Te. Data are shown for 232 NMEs associated with 161 biological targets with exponentiated logistic patterns of maturation enabling estimate of the Te with the TIME model.

Table 3. Duration of clinical development from Phase 1 to approval for NMEs with trials initiated before the underlying technology passed the established point and after that point.

| Type                          | # NMEs                      |           |          | Year from Phase 1 to approval |           |         |
|-------------------------------|-----------------------------|-----------|----------|-------------------------------|-----------|---------|
|                               | Initiation of Phase 1 trial |           |          | Initiation of Phase 1 trial   |           |         |
|                               | all                         | before Te | after Te | all                           | before Te | p       |
| All                           | 117                         | 24        | 93       | 9                             | 11        | 8 ***   |
| <b>Drug subset</b>            |                             |           |          |                               |           |         |
| CDER                          | 114                         | 24        | 90       | 9                             | 10        | 8 ***   |
| CBER                          | 3                           | 0         | 3        | 7                             | -         | 6 n/a   |
| Phenotypic                    | 30                          | 8         | 22       | 10                            | 10.5      | 9 ns    |
| Targeted                      | 87                          | 16        | 71       | 9                             | 9.5       | 8 ***   |
| NCE                           | 73                          | 16        | 57       | 9                             | 9         | 8 *     |
| Biologic                      | 44                          | 8         | 36       | 9                             | 10        | 8 ns    |
| First-in-class                | 58                          | 15        | 43       | 9                             | 11        | 7.5 *** |
| Follow-on                     | 56                          | 9         | 47       | 9                             | 8         | 8 ns    |
| Orphan drug                   | 57                          | 9         | 48       | 9                             | 9.5       | 7 ***   |
| <b>Expedited designations</b> |                             |           |          |                               |           |         |
| Accelerated approval          | 16                          | 3         | 13       | 7.5                           | 5         | 7 n/a   |
| Breakthrough therapy          | 22                          | 1         | 21       | 7.5                           | 5         | 6.5 n/a |
| Fast track                    | 39                          | 9         | 30       | 8                             | 10        | 7 *     |
| Priority                      | 71                          | 13        | 58       | 8                             | 10        | 7 ***   |

Data show for 117 of 356 drugs approved by the FDA from 2010 to 2019. Of the absent compounds, 19 were phenotypic with no known target/mechanism of action, and 105 exhibited TIME model growth patterns that did not fit the exponentialized logistic model. Of the remaining 232 accepted TIME model fits, 117 were matched with a Phase 1 clinical trial start date, thus 'years in clinical trials' could be calculated. Statistical analysis compared the duration of clinical trials (Phase 1 start date to approval date) between NMEs that entered clinical trials before or after the target/technology establishment point (Te) or point of maturity, using the nonparametric, Mann-Whitney U test. With a Bonferroni correction of 14, a difference with a p value below 0.0036 was considered significant (ns – not significant, p<0.0036, \* p<0.0036, \*\* p<0.0007, \*\*\* p<0.00007); n/a – not applicable

underlying bodies of research passed this threshold, and the suggestion that the persistent lags in developing products for Alzheimer's Disease (Beierlein et al., 2015) and gene therapy (Ledley et al., 2014) could be related to the immaturity of essential, underlying research.

Second, Table 3 compares the timeline for clinical development from Phase 1 to first approval for products that entered clinical development before research on the biological target had reached the *established* point and those that entered clinical trials after that point. This is illustrated in Figure 9B. These data show that the clinical development timeline is significantly shorter when the underlying research had passed the *established* point (median 11 years versus 8 years,  $p < 0.0001$ ).

Table 3 also shows that this association was significant for targeted therapeutics, where development is predicated on a mature body of research, but there was no significant association with drugs discovered using phenotypic methods. Moreover, there was no significant association for biologic products, which are classified as “targeted,” but are discovered because of their known biological activities. Together, these results suggest that a mature body of underlying research improves the efficiency of the drug development process and may be requisite for successful product development.

### ***NIH project funding and costs***

As noted in Section 2, the public sector is primarily responsible for funding the basic biomedical foundation that provides the groundwork for drug discovery and development. In the United States, most of this funding comes from the NIH. To assess the NIH's contribution to the research that enabled development of new drugs approved from 2010–2019, we identified NIH funding for published research related to another 219 biological targets described above, as well

as published research directly related to the 356 drugs themselves. This analysis expanded on the study of new drugs approved from 2010–2016 by Cleary et al. (2018) and employed a modification of that method.

The analysis involved recovering the PMIDs for each research publication identified through the PubMed searches for drug targets described above as well as searches performed individually for each of the 356 drugs in this study. PMIDs were identified for the years 1960 through the year of first FDA approval for each drug. When there were multiple drugs against one target, searches included years before the first drug approval. By restricting this analysis to PMIDs published before drug approval, we minimized the number of publications related to the clinical use or marketing of products after approval. PMIDs from searches for each of the 356 drugs (DRUG search) represented research directly related to the approved product and is considered to be applied or translational research. PMIDs from searches for each of the 219 biological targets (TARGET searches) are indirectly related to the drugs and are considered use-inspired, or basic research. PMIDs identified in both a DRUG search and a TARGET search are classified as being drug related. NIH funding for this published research was identified by associating each PMID with NIH-funded Projects (grants) in the NIH RePORTER database.<sup>14</sup> NIH RePORTER includes NIH-funded Projects from 1980-present and identifies publications acknowledging grant funding.

For this analysis, each PMID was linked to a specific Funding Year, representing one fiscal year of the project corresponding to the publication date of the PMID. PMID with publication dates

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<sup>14</sup> The NIH Research Portfolio Online Reporting Tool (RePORT) was created by the Office of Extramural Research at the NIH in 2008 as a repository for information on research funding from the NIH. This data resource includes NIH RePORTER (RePORT Expenditures and Results), which includes data on NIH Projects (grants) as well as publications (PMID citations) and Patents acknowledging support from these grants (<https://report.nih.gov/index.aspx>).

1–4 years after the final year of Project funding were considered to be associated with the final fiscal year of Project funding to account for the observed lags between research funding and publication (Boyack & Jordan, 2011). Data cleaning was performed to eliminate duplicate entries and exclude publications occurring before the first year of Project funding or more than four years after the last fiscal year of funding. Project Costs for each project Funding Year identified in this analysis were derived from the RePORTER database, which has Costs from 2000–present.

**Table 4. Research publications, NIH Funding Years, and Project Costs associated with 356 NMEs approved by the FDA from 2010–2019 or their molecular targets**

|                                                  | DRUG Search    | TARGET Search | Total     |
|--------------------------------------------------|----------------|---------------|-----------|
| <b><u>PubMed search results</u></b>              |                |               |           |
| Searches                                         | 356            | 219           | 574       |
| Unique publications in PubMed (1980–2019)        | 244,327        | 1,977,678     | 2,222,005 |
| <b><u>RePORTER Link table results</u></b>        |                |               |           |
| Unique publications with NIH funding (1980–2019) | 39,099         | 424,192       | 463,291   |
| % publications with NIH funding                  | (16%)          | (21.4%)       | (21%)     |
| <b><u>Totals</u></b>                             |                |               |           |
| Searches with NIH funding                        | 310            | 219           | n/a       |
| Fraction of searches with NIH funding            | (87%)          | (100%)        | n/a       |
| <b><u>Funding Years and Costs</u></b>            |                |               |           |
|                                                  | DRUG           | TARGET only   | Total     |
| Unique Funding Years                             | 63,687         | 515,179       | 578,866   |
| Number of Funding Years with Costs in RePORTER   | 32,972         | 299,052       | 332,024   |
|                                                  |                | \$194,919     |           |
| Program Costs, \$ millions (% total)             | \$35,687 (15%) | (85%)         | \$230,606 |

Table 4 shows the number of research publications, NIH Funding Years, and Project Costs associated with this set of approvals, while Figure 10 illustrates the time course of PMIDs, NIH-

funded PMIDs, NIH funding years, and Project Costs associated with the 356 NMEs or their molecular targets<sup>15</sup> DRUG searches identified more than 460,000 publications, while TARGET searches identified over 3 million publications. Of these, approximately 40,000 PMIDs (16%) identified in DRUG searches had NIH funding in the RePORTER database, while more than 420,000 (21%) of PMIDs identified in TARGET searches had NIH funding in the RePORTER database. NIH funding for publications identified in this work comprised more than 575,000 fiscal years of Project Funding (more than 60,000 fiscal years of research related to the drugs and greater than 515,000 fiscal years of research related to the drug targets). In all, NIH funding was identified for research directly associated with 87% of all the drugs approved from 2010–2019 and 100% of the known biological targets for these drugs (Table 4). In comparison, in our previous work examining new drugs approved 2010–2016, (Cleary et al., 2018) identified NIH funding was associated with 94% of all DRUG searches, likely due to the inclusion of publications dated after drug approval in the earlier study. Importantly, NIH-funded research was associated with every one of the 356 drugs or their biological targets.

This work identified a total of \$230.6B in NIH funding directly or indirectly related to the drugs approved from 2010–2019. Of this amount, \$35.7B (15%) was associated with research identified through DRUG searches, which is considered to be applied research, while \$194.9B (85%) was associated with research identified only through TARGET searches, which is considered to represent basic research.

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<sup>15</sup> Note: the apparent decrease in PMIDs, Funding Years, and Project Costs after 2010 reflects the experimental design in which PMIDs with publication dates after first drug approval were not included in the analysis. Thus, the number of drugs and target searches included in the analysis decreases each year after 2010.



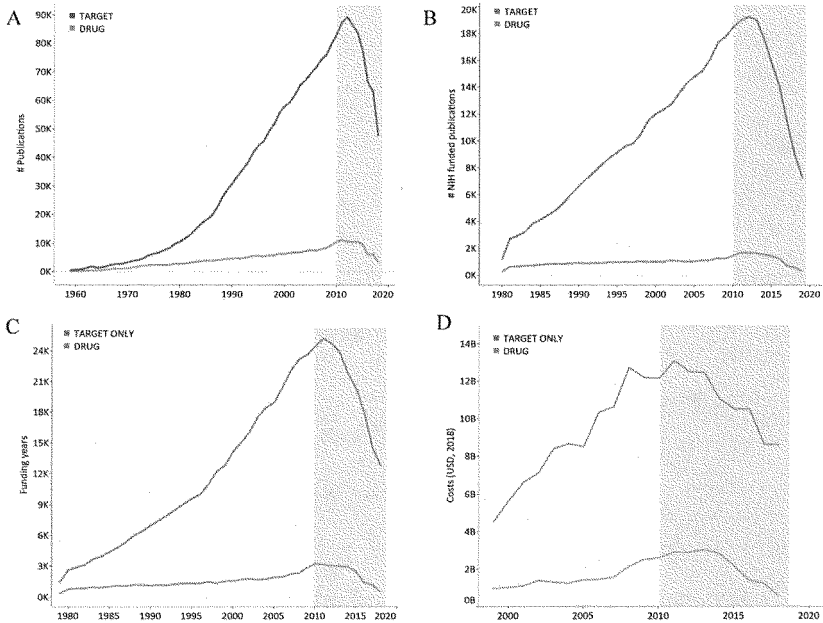


**Figure 10. Number of PMIDs, NIH-funded PMID, NIH Funding Years, and project Costs associated with research on 356 NMEs approved 2010–2019 or their biological targets.** PubMed Searches were performed for 356 NMEs (DRUG search) or their known biological targets (TARGET search). A. Publications in PubMed (PMID) (1960–2019); B. PMIDs associated with NIH-funding in NIH RePORTER (1980–2019); C. Funding Years associated with NIH-funded PMIDs (1980–2019). Funding Years correspond to the fiscal year of funding corresponding to the year of publication or the last year of publication for PMIDs published 1–4 years after the last year of the grant; D. Project Costs (2000–2019). Note: the decrease in PMIDs, Funding Years, and Costs after 2010 is due to the experimental method, which considered only PMIDs published before the date of first drug approval.

### *NIH investment in first-in-class drugs*

To assess the amount of NIH funding that goes into research on a novel drug target before approval of the first-in-class drug associated with that target, we examined the funding for research related to the 136 first-in-class products in this dataset and their biological targets.

**Table 5. Funding Years and NIH Costs associated with 136 first-in-class products.**

|                      | N   | DRUG       | TARGET only | TOTAL       |
|----------------------|-----|------------|-------------|-------------|
| <b>Funding Years</b> |     |            |             |             |
| All                  | 136 | 27,634     | 415,470     | 443,104     |
| Targeted             | 101 | 21,876     | 286,363     | 308,239     |
| Phenotypic           | 35  | 5,758      | 129,107     | 134,865     |
| <b>Costs</b>         |     |            |             |             |
| All                  | 136 | \$16,660 M | \$175,135 M | \$191,795 M |
| Targeted             | 101 | \$13,006 M | \$128,974 M | \$141,980 M |
| Phenotypic           | 35  | \$3,654 M  | \$46,162 M  | \$49,815 M  |
| Costs/NME            |     | \$122 M    | \$1,288 M   | \$1,410 M   |

Of these, 84 were first discovered through targeted discovery and 32 by phenotypic discovery.

Of these, the NIH contributed funding for research related to each of the 136 first-in-class drugs and each of the biological targets. NIH investment associated with these products totaled more than 440,000 fiscal years of grant funding and more than \$190 billion dollars, which is an average of \$1.4 billion dollars per first-in-class drug (Table 5).<sup>16</sup>

#### *NIH investment by therapeutic area*

The NIH investment in drugs for diseases in different therapeutic areas is shown in Table 6. The number of new drugs and NIH Costs was highest for antineoplastic agents. Overall, the number of NMEs in each therapeutic class is strongly correlated with the total NIH spending ( $R^2=.89$ ,

<sup>16</sup> Note: this reflects the total amount of research directly or indirectly related to each first-in-class drug launch. In this analysis, a Project Cost that was related to more than one approved drug would be counted with each product, and therefore counted more than once in calculating total values.

$p<0.0001$ ), but there are notable deviations. While the second largest category of drug approvals was for cardiovascular disease, total NIH spending was larger for anti-infectives, CNS and

**Table 6. Funding years and Costs associated with published research for NMEs approved 2010–2019 by therapeutic area.**

| Therapeutic area       | NIH-funded NMEs | DRUG Costs (Funding Years) | TARGET ONLY Costs (Funding Years) | TOTAL Costs (Funding Years) |
|------------------------|-----------------|----------------------------|-----------------------------------|-----------------------------|
| antineoplastic         | 100             | \$10,629 (9270)            | \$108,407 (198436)                | \$119,036                   |
| anti-infective         | 30              | \$1,684 (873)              | \$61,364 (86852)                  | \$63,048                    |
| central nervous system | 37              | \$1,758 (2130)             | \$48,516 (92045)                  | \$50,274                    |
| immunologic            | 27              | \$2,008 (1541)             | \$42,407 (64074)                  | \$44,416                    |
| cardiovascular         | 47              | \$16,639 (20817)           | \$18,708 (30356)                  | \$35,347                    |
| endocrine              | 8               | \$5,580 (5497)             | \$23,428 (37311)                  | \$29,008                    |
| metabolic              | 31              | \$2,637 (2370)             | \$18,360 (25938)                  | \$20,996                    |
| miscellaneous          | 9               | \$161 (134)                | \$17,720 (29821)                  | \$17,881                    |
| respiratory            | 14              | \$1,888 (1423)             | \$9,931 (16812)                   | \$11,820                    |
| gastrointestinal       | 7               | \$32 (43)                  | \$11,177 (21324)                  | \$11,209                    |

All costs since 2000 in millions USD.

immunological disorders. Similarly, while the second largest category of total spending was for anti-infectives, there were more agents approved for cardiovascular, CNS, and metabolic diseases. There was no significant correlation between NIH spending for TARGET and DRUG research ( $R^2=.22$ , NS). The most notable outlier was cardiovascular disease, which had the largest amount of NIH spending related to DRUGs but ranked sixth in spending on TARGETs.

#### ***Research activities funded by the NIH***

To assess the types of research activities, we examined the Activity Codes of the NIH Projects identified as being directly or indirectly associated with these 356 drug approvals. NIH not only funds traditional, investigator-initiated Research Projects, typified by classic “RO1 funding,” but also funding targeted for small projects (R21), and first-time investigators (R29), and other

specific projects. Each activity is indicated by a unique three-digit Activity Code, with the first letter indicating the Activity category.<sup>17</sup> The NIH also provides funding for Program Project and Center grants, which support research capacity at large research centers, where efficiencies are created by sharing expensive facilities, equipment, and personnel for animal experimentation, analytical chemistry, advanced instruments, large scale production, bioinformatics, and other common research infrastructure needs. Each grant can contribute to the fully allocated cost of research on many different projects. Cooperative Agreements are government-initiated research projects, which often include substantial federal programmatic involvement including government coordination, personnel, or facilities. Other types of NIH funding provide support for graduate students or research fellows, promote diversity in science education or research, or provide career support for accomplished scientists. Such grants provide salary for many of the scientists involved in Research Programs, Program Projects, Centers, or Cooperative Programs, and can contribute to fully allocated cost of research on many different projects. The NIH also supports the research of government scientists at the NIH through Intramural Programs. Figure 11 shows that Funding years and Project Costs categorized by the first letter of the Activity Code. Research Projects (e.g., R01, R21, R29) constituted the greatest number of both Funding Years (66%) and Project Costs (39%) followed by Research Program Projects and Centers (e.g., P30, P50), and Cooperative Agreements (e.g., U01, U09). While the number of Program Projects and Centers and Cooperative Agreements represent a small fraction of the Funding Years identified in this study (8% and 6% respectively), they comprise a disproportionately large fraction of the total Costs (24% and 21% respectively). Several different forms of funding for

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<sup>17</sup> NIH grants are categorized by the first letter of the Activity Code. Activity Codes are: R, Research Projects; P, Research Program Projects and Centers; U, Cooperative Agreements; K, Research Career Programs; Z, Intramural Research; T, Training Programs; D, Training Projects; F, Fellowship Programs; M, General Clinical Research Centers Programs (discontinued 2014). [https://ods.od.nih.gov/research/CARDS\\_lists.aspx](https://ods.od.nih.gov/research/CARDS_lists.aspx).

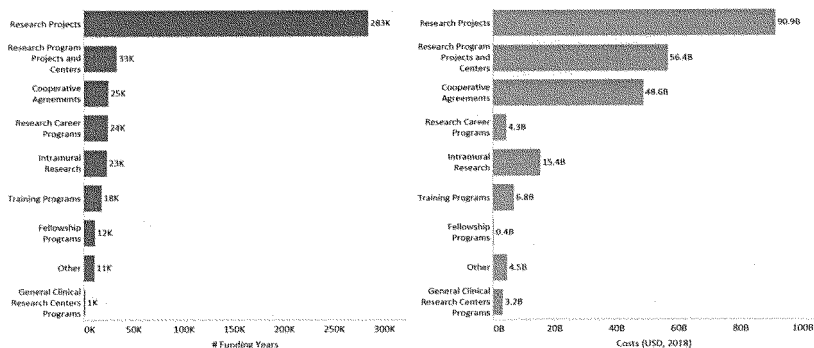


**Figure 11. Funding Years (left panel) and Project Costs (right panel) associated with different forms of NIH funding since 2000.**

training and fellowships contributed smaller fractions of total NIH funding. This analysis suggests that the NIH contribution to drug development does not simply involve funding for investigator-initiated research programs, but also funding for a complex infrastructure of capabilities and personnel required to conduct research. It should be noted that contracts are not included in the RePORTER database, nor are many other NIH contributions to research infrastructure, including construction.

### *NIH-funded patents associated with approved drugs*

Patents were identified in RePORTER associated with NIH Projects that also cited PMIDs identified in DRUG or TARGET searches from 1980–2019. We identified 22,409 such patents representing 17,564 patent families (Table 7). The time course of patent issuance dates is shown in Figure 12. The earliest patents identified in this study were from 1980. The number of patents increased rapidly after 1995, peaking between 1999–2002, then dropping until 2010 when the number increased again. The leveling of the number of patents and decrease over the past two

years is likely due to the experimental method, which only looks at the funding for research published before drug approval and the patents arising from this funding.

**Table 7. Identification of NMEs approved 2010–2019 with patents in the Orange Book funded by NIH-funded Projects also supporting published research on the NMEs or their biological targets.**

| Category                                                            | Patents<br>N | Patent<br>families<br>N | NME<br>(brand)<br>N |
|---------------------------------------------------------------------|--------------|-------------------------|---------------------|
| Patent-IND combinations in the Orange Book (all years) <sup>1</sup> | 49,154       | n/a                     | 2,415               |
| Patents in the Orange Book (all years) <sup>1</sup>                 | 26,579       | n/a                     | 2,415               |
| Patents with NIH funding related to NMEs 2010-2019 <sup>2</sup>     | 22,409       | 17,564                  | n/a                 |
| Patent-IND combinations in the Orange Book <sup>3</sup>             | 1,204        | n/a                     | n/a                 |
| Patents in the Orange Book <sup>3</sup>                             | 567          | 487                     | 144                 |
| NME associated with patents in the Orange Book <sup>4</sup>         | tbc          | tbc                     | 27                  |

(1) Archival data of active and inactive patents from DrugPatentWatch; (2) patents associated with NIH-funded Projects acknowledged in publications on the NME (DRUG) or biological target (TARGET). Many do not include patents from other NIH Projects; (3) includes patents funded by NIH Projects as described in table footnote 2. (4) includes new drugs approved 2010–2019 with patents identified in table footnote #3. n/a - data not available from current datasets; tbc - data to be calculated; Identities between the Orange Book confirmed by matching brand/trade names.

Of these patents, 567 were included in the Orange Book, representing 487 patent families. These patents were associated with 144 different products in the Orange Book (1980–present) and 27 of the products included

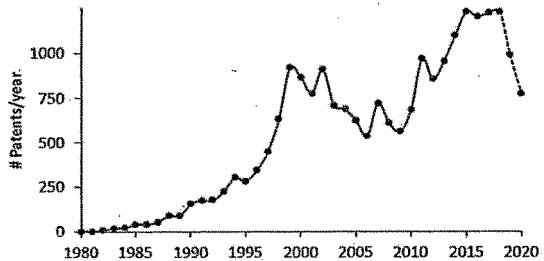


**Figure 12. Number of patents issued/year citing NIH funding also associated with published research on drugs approved 2010–2019 or their biological targets.**

in our study. Of the 356 drugs in our study, 311 were included in the current Orange Book-release (July 2020) or had a patent in the Orange Book from 1980–present.

**Table 8. Percentage of NMEs approved 2010–2019 with patents in the Orange Book funded by NIH-projects also supporting published research on the NME or its biological target.**

| Category                                 | # NME | % NME (3) |
|------------------------------------------|-------|-----------|
| NMEs 2010–2019                           | 356   |           |
| # listed in the Orange Book <sup>1</sup> | 311   |           |
| # with patent in the Orange Book         | 295   | 95%       |
| # with NIH-funded patent <sup>2</sup>    | 27    | 8.7%      |

(1) Includes NMEs with patents in the Orange Book as well as NMEs listed in the Orange Book accessed 7/2020. Does not include CBER drugs and some biologic products removed from the Orange Book in 3/2020. (2) Includes drugs with patents associated with NIH-funded Projects acknowledged in publications on the NME (DRUG) or biological target (TARGET). Many do not include patents from other NIH Projects. (3) Percentage of NMEs with confirmed listings in the Orange Book either from complete patent list or search of 2010–2019 NME approvals performed July 2020.

Of these, 295 (95%) had at least one patent in the Orange Book and 27 had a patent in the Orange Book that was associated with the research identified in this study (Table 8). This fraction is similar to the fraction of drugs with NIH-funded patents in the Orange Book identified using a variety of other methods (Li et al., 2017; Long, 2019; Sampat, 2006; Sampat & Lichtenberg, 2011; Stevens et al., 2011).

We would caution that the Orange Book only describes patents that are considered to provide marketing exclusivity to FDA-approved products, and represents a legal assessment rather than a business or technical measure of the importance of specific research to product development. Thus, the Orange Book does not necessarily describe all of the intellectual property that may

have been acquired or licensed in the course of product development, nor all of the intellectual property that may generate royalties from product sales.

### ***Limitations of this research***

There are several major limitations to this research. First, this analysis is limited by the quality of the search algorithms used to identify PMIDs associate with the drug and drug targets. While considerable optimization of the search terms was performed, all three methods utilized—Boolean searches, MeSH subject headings, and Automated Term Mapping—were found to be inconsistent in their sensitivity and specificity. Second, the RePORTER database has incomplete data from some agencies within HHS and there is considerable missing data. In addition, the association of PMID publication dates with specific Funding Years is imperfect. Even with the correction for the lag of publication activity after the last year of a funded Project, up to 10% of publications are not associated with a specific Project Year or Cost. Third, many of the phase initiation dates were not available from public databases, particularly for Phase 1. The PharmaProjects database had Phase 1 start dates for only 117 of 232 drugs with accepted TIME fits. While we were able to fill in missing Phase 3 start dates from ClinicalTrials.gov, this database has little or no coverage of clinical trials prior to 2007. Fourth, identification of drugs in the Orange Book requires text matching to brand/trade or generic/ingredient names and can be incomplete. In addition, the association of drugs with patent numbers can be compromised by the removal of patents from the Orange Book at expiration. Finally, as discussed above, we would caution that the NIH funding identified in this research does not represent the per/drug cost of research or development leading to drug approval, but rather the NIH contribution to the ecosystem necessary for enabling this development.



### 3. Conclusions

This Working Paper quantifies NIH funding for basic or applied research related to each of the new drugs approved by the FDA from 2010–2019. It extends previous analyses of the published research related to drugs approved since 2010 or their biological targets, the NIH-funded Projects (grants) that are acknowledged by these publications, and the Costs that contributed to this research (Cleary et al., 2018; Cleary & Ledley, 2020). It also examines the maturation of this published research over time, the impact of technological maturation on the efficiency of product development, the nature of the NIH funding supporting this research, and the patents that arise from this work. By detailing the role of the public sector in pharmaceutical innovation, we hope to inform evidence-based policies aimed at accelerating the translation of scientific discoveries for public value, achieving the “*highest attainable standard of health*” for the public, and provide insights into the public sector’s role in value creation and equitable distribution of this value.

This study focuses specifically on the role of the NIH, whose annual budget of \$40 billion (Sekar, 2020) makes it the largest source of public sector funding for biomedical research in the world. We examine this role in the context of a linear model of innovation. Without critiquing the theoretical or evidential underpinnings of the linear model or its indisputable limitations, this model has had a central place in the formulation of contemporary science and innovation policy. The longstanding distinctions between basic and applied science, the division of basic and applied science between the public and private sectors, and the construction of the Bayh-Dole Act are each reflections of this model.

So too, are some of the critical policy challenges facing biopharmaceutical innovation. These include: the uncertain sustainability of public sector support for basic biomedical research; the

short-term perspectives and shareholder focus of an increasingly financialized biopharmaceutical industry; the asymmetrical distribution of risk and reward between the public and private sectors; the adverse impact of high drug prices on the affordability and availability of essential medicines and, consequently, public health; and the lack of any effective mechanisms for public oversight over the development enabled by public investment in the earliest stages of scientific and technological innovation.

The overriding observation in this work is the magnitude of the public sector contribution to biopharmaceutical innovation. We identified more than \$230 billion in NIH grant support (2000–2019) for research directly related to the 356 drugs approved over the last decade or their biological targets. Of this amount, more than 85% is classified as basic science related to the biological target, rather than the drug itself.

This is consistent with the expectation embodied in the linear model of innovation that public sector investments are principally focused on the basic science that precedes applied or translational science, rather than product development. Also consistent with this model is the fact that every one of these drugs was brought to market in the United States by a biopharmaceutical company, rather than by an academic, governmental, or non-governmental organization.

The more than \$230 billion in NIH research support represents a significant fraction of the NIH's total \$586 billion budget allocation<sup>18</sup> over this interval and needs to be interpreted in context of the methods used in this analysis. Our method does not focus on discrete developmental milestones such as “target discovery,” “target validation,” “first synthesis,” or “final molecule”

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<sup>18</sup> National Institutes of Health Actual Total Obligations by Budget Mechanism, FY 2000–FY 2019 ([https://officeofbudget.od.nih.gov/pdfs/FY21/spending-hist/Mechanism%20Detail%20for%20NIH%20FY%202000-FY%202019%20\(V\).pdf](https://officeofbudget.od.nih.gov/pdfs/FY21/spending-hist/Mechanism%20Detail%20for%20NIH%20FY%202000-FY%202019%20(V).pdf)).

as, for example, in the work of Eder et al. (2014), or cast studies of product development (Chakravarthy et al., 2016; Cockburn & Henderson, 1996, 2000; Nayak et al., 2019). Nor is our analysis restricted to research associated with utility patents (Li et al., 2017; Sampat, 2006, 2009; Sampat & Lichtenberg, 2011; Stevens et al., 2011). We believe that such methods, which focus specifically on research with applications to specific products, systematically underestimate the public sector's role in supporting basic science, which may not be explicitly associated with any individual product.

Our method aims to describe the public sector's contribution to the broad ecosystem required for biopharmaceutical innovation. It posits that the full body of published research—research comprising dramatic new discoveries, details of biological structures of functions, deconstruction of failed experiments, or duplication of seminal results—contributes to advancing the “forefront of knowledge” that enables drug discovery. This approach recognizes the inherent complexity of biological systems and the need for a systems approach in drug discovery and development (Butcher, Berg, & Kunkel, 2004). It also recognizes the challenge of anticipating “unknown unknowns,” which may not be on the critical path for development, but can contribute to idiosyncratic or irreproducible results in preclinical or clinical studies (Mullane & Williams, 2015).

Our previous work has shown a consistent relationship between TIME metrics for the maturation of research on discrete biological targets and the efficiency of developing products based on this research (Beierlein, McNamee, & Ledley, 2017; Beierlein et al., 2017; McNamee & Ledley, 2012, 2017; McNamee et al., 2017). The present work extends these observations in a substantially larger dataset, showing that none of the products with targets that can be modeled with the TIME model were approved before research on the target passed the analytically

defined *established* point of maturation. Moreover, the timelines of clinical development were significantly shorter when clinical trials began only after this point. These data provide further confirmation for the concept that an *established* body of basic research, defined in this work as publications on a drug’s biological target but not the drug itself, is requisite for successfully developing new medicines.

In the linear model of innovation, most of this enabling basic research is largely the domain of the public sector. While the private sector may invest more than a billion dollars in each new product that is successfully developed (DiMasi et al., 2016; Wouters et al., 2020), this work suggests that the public sector contribution to the early stage research that precedes and enables development may be of the same order of magnitude. This is consistent with the role of the public sector as the “early investor” or “investor of first resort” in the earliest stages of biopharmaceutical innovation and value creation (Block & Keller, 2015; Hopkins & Lazonick, 2014; Lazonick, 2017; Lazonick & Mazzucato, 2013; Mazzucato, 2011, 2016; Mazzucato & Semieniuk, 2017).

Our analysis illustrates the complexity of properly accounting for this public sector investment due to the broad spillovers of public sector research among many different products. Specifically, we observed that PMIDs and Project Years identified in this analysis were associated with more than one new drug, biological target, and even therapeutic area. In fact, the complexity of this analysis arises from the extensive duplication of PMIDs, Project Years, and Costs in the core dataset.

We previously characterized spillovers in a study of the 59 new cancer drugs approved from 2010–2016, in which we found that much of the research directly related to new cancer drugs or

their biological targets was not funded by the National Cancer Institute, nor was it explicitly identified as “cancer research” in the NIH’s Research Condition Disease Categorization system. Rather, we found that much of this research was funded by institutes with disease-specific missions outside of cancer, which had spillover applications to malignant disease (Cleary & Ledley, 2020). For example, more than \$1 billion of this research was funded by NIAID, NHLBI, and NIDDK. The present work suggests that such spillovers are also evident in the patents that result from NIH-funded research. Specifically, while only 27 of the drugs in our study had patents in Orange Book patents arising from Projects identified by the DRUG or TARGET searches, many of these patents were listed in the Orange Book in association with drugs that were not part of this study. While we have not fully characterized these products, this is further evidence for the spillover of basic science to many different product opportunities.

One reason for this spillover may be that while the large majority of Projects identified in this study (66%) supported investigator-initiated Research Projects, these Projects accounted for only 39% of the total Costs. The combined Costs of Research Program Projects and Centers, Cooperative Agreements, and programs for training and fellowships were greater. These other forms of NIH Project funding do not support investigator-initiated research, but rather provide the infrastructure, technological, human, and organizational capabilities necessary for this work. The Costs that were identified as contributing directly to research related to drugs approved 2010–2019 or their biological targets likely also contributed to research related to many other products as well as future innovations.

The importance of spillovers from a broad foundation of basic research was evident in the rapid identification and Emergency Use Authorization of Remdesivir as a treatment for COVID-19 only four months after the virus was first discovered. Using the same methods employed in this

study, we demonstrated that the NIH had invested \$6.5 billion in research that could be related to the biological target for Remdesivir (RNA dependent RNA polymerase) or the pharmaceutical chemistry underlying its chemical structure (a nucleoside analog) even before the virus had been discovered. Significantly, only 12% of the NIH Costs identified in that study were associated with investigator-initiated Research Projects, while 34% was for Research Program Projects and Centers and 40% for Cooperative Agreements (Cleary et al., 2020). Thus, the ability to quickly identify a potential treatment for an unanticipated pathogen represented a spillover of research on other disease indications or drugs as well as the power of a robust, public-sector funded infrastructure for biopharmaceutical innovation.

The importance of spillovers is one reason that investments in basic science are unattractive to pharmaceutical companies. While there is evidence that investment in basic research can provide a positive return on investment (Toole, 2012), the benefits of this investment do not necessarily accrue to the firm that funded the basic work. Similarly, spillovers complicate effective accounting for the public sector contribution to the value created by novel pharmaceutical products.

This analysis highlights the inadequacy of the Bayh-Dole formula for recognizing the public sector contribution in the earliest stages of drug discovery and development and a return on its early-stage investments in biopharmaceutical innovation. This work demonstrates that, despite the fact that we identified NIH funded research directly or indirectly related to every one of the new drugs approved 2010–2019, only 8.6% of these drugs had patents listed in Orange Book that were explicitly based on this research funding. While many other patents may contribute to the discovery, development, or production of these products, those listed in Orange Book have the

most tangible impact on the financial returns of the pharmaceutical manufacturer. By conventional measures of financial accounting, these are therefore the most “valuable.”

It is harder to recognize the value of non-patented intellectual contributions, such as know-how, or trade secrets, and knowledge placed in the public domain through academic publications. Even if such intellectual property were acquired by a pharmaceutical company, such as by funding academic research or acquisition of an early-stage biotechnology company, it would be treated as an intangible or impaired asset, and recognized as an expense that reduces earnings rather than a valued asset. While this distinction may be semantic in the context of this analysis, such categorizations are completely contrary to the essential role that such intellectual contributions play in enabling drug discovery and development.

Moreover, the Bayh-Dole Act has only limited applicability to advances in biomedical research that do not generate patents. The Bayh-Dole process is initiated by disclosure of a “subject invention”<sup>19</sup> by the recipient of a government grant. This disclosure triggers various reporting requirements to the government, steps towards the patenting and licensing of the invention to industry for development, and certain government rights including the right to practice the invention and “march-in rights” under specified circumstances (Thomas, 2016).

The large majority of the NIH funding identified in this study, however, resulted in publications that were categorized as “basic research.” Basic research is not expected to generate results related to the “utility” and “enablement” of any specific products. As much of this research does not generate patentable subject matter, would not trigger a subject invention disclosure, and the

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<sup>19</sup> “Subject invention” is defined in paragraph 401.2(d) of the Bayh-Dole Act: “The term subject invention means any invention of a contractor conceived or first actually reduced to practice in the performance of work under a funding agreement;” [https://grants.nih.gov/grants/bayh-dole.htm#se37.1.401\\_18](https://grants.nih.gov/grants/bayh-dole.htm#se37.1.401_18)

Bayh-Dole process designed to ensure the creation of public value in the form of both new products and payment to the public sector would not apply. Without addressing the strengths and limitations of Bayh-Dole (Bremer, Allen, & Latker, 2009), no other mechanism currently exists to govern the translation of scientific discoveries for public value in the form of new products, better health, job creation, or economic growth or provide for government oversight or rights related to this process.

Finally, it should be noted the process of biopharmaceutical innovation is increasingly moving away from the linear model on which Bayh-Dole is based. No mechanisms currently exist for recognizing the value created by public sector investment in translational science (Collins, 2011; Varmus, 2006; Woodcock et al., 2014), the “entrepreneurial university” (Etzkowitz, 2016, 2017), or the triple helix of government-academic-industry collaborations (Leydesdorff & Etzkowitz, 1998).

Lazonick and Mazzucato (2013) have examined what they term the “Risk/Reward Nexus” of innovation and the mechanisms that lead to asymmetrical sharing of risk and reward between the public and private sector. They illustrate this asymmetry with the observation that the *“blockbuster biotech drugs that generated huge returns for both big pharma and biopharma companies reflect control over patent rights to the ‘low-hanging fruit’ that became available to these companies in the 1980s as a result of decades of NIH funding.”* Our work highlights both the scale of the “risk” being taken by the public sector as an early investor (Mazzucato, 2011, 2017) in pharmaceutical innovation and the complexity inherent in ensuring that this investment is properly rewarded. It also demonstrates the need for innovative policies that ensure the public sector investments in science are efficiently translated into public value, not only in the form of new products, job creation, and economic growth, but most importantly public health.



Mazzucato has written that *“a better understanding of the role that the state has and can play in the wealth-creation process is the starting point for policy solutions that can increase the rate of wealth creation”* (Mazzucato, 2017). We hope that the data in this Working Paper will lead to new insights into evidence-based policy solutions that fully realize the value of public sector investments in pharmaceutical innovation that ensure that they lead to meaningful improvements in health.

## Appendix

### Technology Innovation Maturation Evaluation (TIME) model

The bibliographic Technology Innovation Maturation Evaluation (TIME) model fits the cumulative number of publications from a technologies Boolean PubMed search results to an exponentiated logistic function as described previously (McNamee, Walsh, & Ledley, 2017).

The exponentiated logistic function equation has the form:

$$N = L \left( \frac{1}{1 + e^{-r(t-t_0)}} \right)$$

Where N is the number of publications, L is the predicted upper limit of publications, r is the growth rate, t is time (year), and  $t_0$  is the midpoint of the exponential growth phase. This asymmetric sigmoidal function exhibits the common logistic sigmoidal function over log scales. The parameters were fit to time series publication data using a non-linear least squares implementation of the Levenberg-Marquart algorithm (LMFIT, version 1.0.1). This results in a technology having a symmetric growth phase that is exponential on average. The initiation (Ti) and established (Te) points, representing the beginning and end of this exponential growth of an individual target/technology, or  $\log N''(t)_{\max, \min}$ , can be analytically determined by:

$$\text{Established, Initiation} = t_0 \pm \frac{\text{acosh}(2)}{r}$$

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Mr. POCAN. And then, finally, very quickly, Dr. Collins. If you had 10, 20, 70 billion dollars more, literally, what would that mean as far as research, and what new areas would we be going to, in a very quick amount of time?

Dr. COLLINS. What a lovely question. You know, a lot of it would be basically that we could provide for this amazing research workforce that is out there the opportunity to pursue all kinds of ideas that we currently can't quite get to. We are still only funding about one grant application out of five, and I know we are leaving really good science on the table when that happens. To be healthy, really, to take advantage of all that creativity, it ought to be at least one out of three.

So that would be a big part of what I would do, and I would particularly focus on those early stage investigators. They are our future. They are the ones that are most vulnerable when things seem a little tight, and we would want to be sure that they felt this experience to be something that was going to be sustainable and, particularly, if they come from diverse backgrounds where we have this need, as we have been talking about in this whole hearing, to enhance the ability of all those different voices to come and join us, to make their careers out of biomedical research and for us to sustain them. That is what I would want to do is just make sure the whole landscape is advantaged by this kind of opportunity.

Mr. POCAN. Thank you very much. And working towards that with DOD, but we will get back to you on it. And I yield back, Madam Chair.

The CHAIR. Thank you.  
Congresswoman Cline.

Mr. CLINE. Thank you, Madam Chair.

Let me start with a question for Director Collins. There was an NIH OIG report from January of last year that found that NIH resolved 262 of the 487 audit recommendations that were outstanding during fiscal year 2015 and 2016. However, it did not resolve about 63 percent or 166 out of the 262 recommendations within the 6-month resolution period required. In addition, as of September 30 of 2016, NIH had not resolved 225 audit recommendations that were past due for resolutions. Are you familiar with this report, Director Collins?

Dr. COLLINS. This is a report about our IT systems and cybersecurity.

Mr. CLINE. It is several different audit recommendations, but the OIG report, yes.

Dr. COLLINS. So, yes, I am very familiar. And we have worked hard working with IG to respond to those. And I think actually a lot of work got done that doesn't necessarily get reflected in that report in that we inspired actions across the board. And the actual numbers now of responses would be considerably better than what you have seen there.

So, yes. I think all organizations are struggling a bit with this. Many of us have had government agencies that have been around a long time, and the new era of cyber security is challenging us, and we are going to need more resources for that as well in order to try to be sure we are doing everything we can to keep the bad actors out of our systems.

Mr. CLINE. Well, I was pleased to find that a March 2020 OIG report found that NIH successfully checks all applications to identify instances of duplicate grant funding. As funding levels are increased and new grants are established, the Federal Government does continue to grow. This dramatic increase in Federal spending is of great concern, and I am reminded of a quote by Milton Friedman, who said, nothing so permanent as a temporary government program. Can you answer what safeguards you are putting in place that work to eliminate duplicative funding for NIH?

Dr. COLLINS. We have worked hard on that, Congressman, because we are in agreement. Every dollar that the taxpayer is providing, that you, the Congress, gives to us needs to be considered as something that we hold a great deal of responsibility for. We are able, through our now very much far advanced portfolio analysis system, to see exactly what is in our portfolio, what we are funding. And we can compare what is in our grant portfolio with other agencies, like the National Science Foundation, like ARC, like Department of Defense, identifying if there are instances where somebody is basically trying to double dip. And if we find those, obviously, we are going to take appropriate action. So I think I can reassure you that we are on top of that using a lot of the latest tools for doing text mining to discover things like that.

Mr. CLINE. All right. Thank you, Madam Chair. I yield back.

The CHAIR. Thank you.

Congresswoman Frankel.

Ms. FRANKEL. Hello. Thank you again. I have a couple of questions.

First, I think this would go to Dr. Sharpless. Gynecological cancers are impacting millions of women each year, yet I am told that we are experiencing declining NCI funding levels and that there is a very huge disproportionate amount between what is funded for, for example, prostate cancer versus ovarian, cervical, and uterine cancer. It is almost like—I will just give one example. Not that I want less for prostate cancer. That is not the point here. But \$1.8 million per person, a year's life lost for prostate; ovarian, \$97,000. So I guess really the question is, do we need more money for research for women's gynecological cancers?

Dr. SHARPLESS. Thank you for raising the issue, and this is something we have looked at carefully. I share your concerns about, you know, funding major diseases like endometrial cancer, ovarian cancer, and cervical cancer. I think, you know, if you look at our GYN portfolio, there are some really strong areas of progress but also some areas where we need to see more attention. I would say endometrial in particular is an area that we have spoken to the community about and heard a lot about where I think we can do more.

We have seen some really remarkable progress in these areas, you know. Our networks enrolled something like 675 women on GYN oncology trials. We have these specialized programs of research excellence, these large grants. And I think we have seven of those now dedicated to gynecological malignancies, including five in ovarian cancer. So I think that, you know, we have to take the opportunity to fund where the scientific availability is, but, you know, it is certainly an area that we are watching closely.

Ms. FRANKEL. I hate to interrupt, but do you need more funding for that kind of research? That is the question.

Dr. SHARPLESS. Well, you know, I think as I answered earlier, we have a lot of grants that we can't get to, you know, and we certainly have a lot of great gynecological malignancy grants in that pool of moneys that we are unable to get to. So, yes, I think more funding for gynecological malignancy research would be very much appreciated.

Ms. FRANKEL. Okay. So, if you could just follow up with, like, an amount, that would be helpful.

Dr. SHARPLESS. Sure.

Ms. FRANKEL. I did have another question, Madam Chair, but I guess I don't really have time for it. There are only 32 seconds. Okay. You are going to let me ask it. Well, here is the thing. No. I guess you are not going to let me ask it.

The CHAIR. I am not going to let you ask it. I thought you were waiting for an answer from Dr. Sharpless.

Ms. FRANKEL. Dr. Sharpless, do you want to answer that question? How much more do you need?

Dr. SHARPLESS. Well, we will provide that to you, that number to you? Let us give it thought.

Ms. FRANKEL. Okay. Thank you so much.

Now I yield back, Madam Chair.

The CHAIR. Thank you very much.

Congresswoman Watson Coleman.

Mrs. WATSON COLEMAN. Thank you, Madam Chair.

Tackling onto what Lois just said, I agree. I support additional resources in this area, particularly concerned about issues of the disparity in outcomes in health as it relates to some of these issues like uterine cancer, like cervical cancer, and its disparate impact on Black women; like sickle cell anemia, when are we going to be able to really be able to tackle this disease; and also maternal and infant mortality and morbidity. I just kind of want to lay them on the table. I know they are of concern. Some of them have been mentioned. I just need to know that they are a part of the priorities, even with all the competing needs and requests, that these issues of disparity in healthcare and in outcomes to minorities in particular are your top—are one of your top priorities.

And, Dr. Collins, you can just answer for everybody.

Dr. COLLINS. I can speak for everybody. Absolutely, yes, and you will see when the President's budget is fully fleshed out in a couple of days that health disparity research is going to be one of the most highly prominently featured areas that we want to do more.

Let me just quickly ask Dr. Bianchi to say something about maternal mortality because we haven't talked about it at this hearing, and we have this program she can tell you about called INCLUDE, which I think is really important.

Dr. BIANCHI. No. IMPROVE, not INCLUDE.

Dr. COLLINS. Yeah. That is right. I got the wrong acronym.

Dr. BIANCHI. Maternal Health and Pregnancy Outcomes Vision for Everyone, and this was in response to the meeting we had prepandemic with the Black Maternal Health Caucus, where we were challenged to do something, and, indeed, we did. And last time when I came to this committee in early March of 2020, we in-

roduced it. But since then, we have funded over \$7 million in grants addressing disparities in maternal morbidity and mortality, and we as an institute are very committed to this. We are the largest funder in maternal health research.

And just as an example, in California, research that we funded implemented a quality improvement to address obstetric hemorrhage, which was an area of major disparity between Black women and White women. And by implementing 17 recommendations, the rate of severe morbidity in Black women went down by 9 percent. So it had—

Mrs. WATSON COLEMAN. I know that there is a lot being done. I want you to know I need to give New Jersey a shoutout. Our first lady, Tammy Murphy, and our Governor, they have made this a priority in New Jersey. And I am sure they are looking for the funding, but they are also looking to be a model. Thank you so much, and I yield back.

The CHAIR. With that, let me yield to the ranking member for any closing remarks as he would like to make.

Mr. COLE. I am sorry, Madam Chair. It took a minute to unmute. You came to me faster than I anticipated. I am very happy to have the opportunity.

First, I want to begin by thanking you for this hearing. It is wonderful to hear how many members on both sides of the aisle say, "This is my favorite hearing of the year." And more profoundly, I want to thank you for your partnership over 6 years in the majority and the minority in working to increase the resources available to the NIH.

And I think your questions and some of the responses we got, certainly from Dr. Collins and others, showed what a difference this subcommittee has made by prioritizing this particular investment for the American people. It has saved a lot of lives, you know, in a variety of ways, but certainly in the pandemic that we have been going through.

I am really proud of what this committee did, and I am very proud of what the NIH, more profoundly, accomplished in this year, not only for us but for all of humanity. Everybody in the world benefited from this investment. So I am pleased and proud about that.

I also want to do something that is probably a little unusual. I want to associate myself with the remarks of Mr. Pocan. We don't agree on everything; we agree on this. If we could do additional resources here, that would be wonderful. Although, again, I really want to point out, I am very pleased with what the administration has proposed as a top line. I have some questions about how we should distribute those funds and whether ARPA-H should get, you know, exactly the amount we are talking about or we should put that to more traditional things and let this initiative grow, but those are matters of discussion and debate. They are not matters of disagreement. And so I certainly will be working hard with you to see that we reach these top lines because I think they are really important for the American people.

I will disagree with my friend from Wisconsin on one thing. It shouldn't come at the expense of defense. And I just say this as an old historian. Look. The cost of great power rivalry in history is



very high, and we should not underestimate the kind of world we live in today with China and Russia. It is a dangerous world.

So we can debate, and we will in another forum, what is appropriate for defense. I don't think that investment there, whether it is as high as I would like or lower as others might prefer, should interfere with this investment because I think this investment is as important for the health and security of the American people as any other that we make.

So I am going to be working with my friend, the Chairwoman, to try and get the maximum number here and certainly working with the administration where I have some disagreements, as I have expressed in other areas, but we don't disagree here. And I am very pleased to see the President actually, you know, frankly stepping up to Congress.

My friend, the Chair, and I have talked about this before. Congress has been the leader in this area for, not a few years, but for generations. It has been Congress that has made these investments. I always tell people I think it is because we are at townhall meetings, and we interact more with people that tell us about their challenges in their family with cancer, their challenges with Alzheimer's or what they have seen a friend at church or at work or at their civic clubs go through in terms of chronic illness. And I think we feel that collectively, Republican and Democrat, very deeply, and I think that is why this committee has done what it is done over many, many years.

And, particularly, though, I am proud of my association with you, Madam Chair, over what we have done in the last 6 years. So I would just say, number one, thank you for the hearing. It is always a great hearing. Much more importantly, thank you for your commitment in this area. It is well known and widely appreciated on both sides of the aisle.

And I want to thank Dr. Collins and his associates at the NIH. We really appreciate the work that you and your colleagues do. We really appreciate not just the immediate science but the thoughtfulness about what it takes to create an infrastructure of science, if you will, where we are attracting young researchers, where we are, you know, presenting people with the opportunities to good science.

I think about what our good friend, Dr. Sharpless, said about cancer in particular. You know, it is a great thing to go from 8 to 11 percent, I guess, funding the proposals, but it is 11 percent. None of us should be excited about that. I can assure you not every one of the proposals we didn't fund is good science, but a lot of them are, and we lose over 600,000 people a year, 650,000, as I recall, to cancer. That is as much as COVID, you know. That is on an annual basis, and that is with a 65-percent recovery, rate which is something this committee in particular can be proud of when it is done, but we need to do more.

So let me just end with this: What a great hearing. I want to thank all the members, you know. Their participation was great on both sides of the aisle. I want to thank you, Madam Chairwoman, for holding it. I particularly want to thank Dr. Collins and his colleagues at the NIH. I think most Americans probably don't realize what an extraordinary thing we saw in the last year. The idea that we could create in this country in less than a year multiple vac-

cines for a pandemic is an extraordinary achievement. NIH wasn't the only player in that, but they were the quarterback in the big game, and they were a major player all the way through. I particularly appreciate Dr. Collins pointing out how the previous investments of this committee over multiple years and multiple iterations of who was in control have really made a difference for the American people. This is something, and we have talked about this many times, Madam Chair, where we need sustained, annual, above-inflation increases. We have achieved that all 6 years you and I have worked together. It is very much my hope we will achieve that again as we go forward. I think it is really in the interest of the American people, and, frankly, in this case, in the interest of all humanity because the engine of the NIH does a lot more than just help us here in this country. I think the best thing we can do, you know, diplomatically in terms of our geopolitical situation is just help people around the world. It is a wise investment, whether it is in foreign assistance, whether it is the science that is made available here. I do associate myself with my friends who are worrying about the decision to, you know, willy-nilly give away intellectual property. I personally think that is a mistake, but I think the instinct behind helping people beyond our own borders is something that we should be proud of and something an asset for our country.

So, with that, Madam Chair, again, thank you for a great hearing. I am sorry I won't be with you tomorrow, believe me, in multiple ways, but I appreciate very much again this hearing. Not only this hearing, the sequence of hearings you have put together. They have been spectacular for this committee. And, with that, I yield back to my friend.

The CHAIR. Thank you very, very, very much, and I will miss you tomorrow. I will miss you. And I thank you. I think you have, you know, laid out both how we sustain what is happening, how we really, in effect, utilize this opportunity to build that architecture for the future, you know, that we need because this is about the noble mission of saving lives. That is where we—you know, there isn't a greater goal or a mission of anything that we do at the Federal level as what is really accomplished through the NIH.

I do believe that Congresswoman Lawrence is still here, and she didn't get a chance. If you had a quick question or a quick comment, Congresswoman Lawrence, because we need to wrap up.

Mrs. LAWRENCE. Yes. I wish that the system hadn't gone down. I just want to express this concern, that I was so impressed at the response and all hands on deck when it came to fighting this virus. But as you have heard from multiple members, there is, for me, the impression that it is just business as usual with some very chronic diseases like cancer, hypertension, and other diseases that we know is what they call the underlying conditions. Where is it—is it more money needed? Is it the direction of leadership that we can keep this overall—Dr. Fauci, I mean, you led the way of not allowing any stone unturned, and I feel that our science in some of these critical diseases, dementia and others, we are not getting the same amount of a sense of urgency. Can you address that? Is it money? Is it—what is it that we need to do?

Dr. COLLINS. So let me take a first stab at that, but Tony may want to add. I think you put your finger on exactly the reason why we think at NIH, there are two major things we need to push harder in this coming year: health disparities research being one, and mechanisms to be able to do that more aggressively, more nimbly, more in a different way of actually trying to achieve results. And that is where this ARPA-H model actually fits in. And I don't think I have said it until now, and I should have. ARPA-H also offers opportunities to pursue problems like the ones you are mentioning, the chronic illnesses, diabetes, hypertension, that cause health disparities, and we would aim to use that engine for that purpose as well. I have had many ideas already brought to me about what we might be able to do with that mechanism that our traditional method of grant giving can't quite achieve at the same timetable.

Tony, I don't know if you want to add something because I think she really addressed the question to you.

Dr. FAUCI. Well, you know, Congresswoman Lawrence, it goes well beyond the NIH. So not to pass the buck to others, but I think it is important, what you point out, that the COVID-19 pandemic has shown a bright light on these kinds of disparities which are really due to literally decades-long social determinants of health that start from birth. As you mentioned in a very articulate way in your presentation, from diets that are not available to people to not getting your hypertension diagnosed when you are young and to present when you have already scars of hypertension and renal disease and heart disease.

There are things that we can do at the NIH, but I hope that the rest of the world and the rest of the country specifically realizes that this is a decades-long commitment to remove those social determinants that are really part, as Dr. Collins said in his opening remarks, part of the racism that has existed in this country for such a long period of time.

Mrs. LAWRENCE. Thank you. I just want to say that we really need all hands on deck on this, and thank you for everything you have done with COVID. Thank you.

I yield back.

The CHAIR. Thank you. And let me just—I am just—I will wrap up, but I want to just say to my friend, the ranking member, Congressman Cole, I think about how blessed we are that we are serving in the United States House of Representatives, that we are part of an effort, and particularly with this subcommittee, where we have come together over the last several years and increased NIH funding by \$12.9 billion, 42 percent over the last 6 years. We did it in a collaborative way. And it is not just to give lip service to being bipartisan, but it is genuinely understanding the value of the research that is done at the NIH.

And, you know, we often think about we are in these positions, you know, and it is what you do with a position, that you come to understand why you come to serve. And I know why Congressman Cole has come to serve, and that is to make the institution work for the benefit of people that he represents, but for the entire country, and yes, in this context, for humanity.

So it is really an honor and a pleasure to be able to work with him on these issues because there is such a commonality of purpose and, you know, a sense of a moral responsibility to be able to get these—to be able to get things done and to provide the resources that this committee has to be able to get these efforts underway and to fruition.

I want to say a thank you. I would just say to you, Dr. Sharpless, I know that your sleepiness, you are staying up at night, I think it could be resolved and remedied by resources. So I think that that is what, you know, I picked up during the course of your exchanges with our colleagues today.

But to all of our witnesses here today, it is exhilarating. I don't know how best to say it. It is exhilarating. And my hope and yours is that we are together next year in person. I believe that we will. And one of the reasons why this is the most important hearing, in my view, that we have is because what we do is we learn of the discoveries to cure that you are engaged in and what you are doing. What is it that we learn? What your future research will result in, what it can do. And we know that the resources that we provide for a specific area can, in fact, lead to the discovery in so many other areas. And it is all with the goal of saving lives. And as I said a few moments ago, there isn't any more important mission.

I always say, you know, I represent, you know, a State that deals with helicopters. We deal with roads. We deal with bridges. We deal with all kinds of issues. But nothing is more important than the content of what is the subject matter of today's hearing. I will again repeat: The tremendous success of COVID-19, the mRNA technology. Listen. This is the biomedical research that you have been working on, and you never know. You can tell us better than we can tell you because we are not scientists. You never know where the years and the decades of basic research are going to take you, where the breakthroughs are going to be made. And in that context, I reiterate the importance of continuing to support sustained increases in funding for basic research at NIH. None of the successes that we have discussed today would be possible without that basic research.

So, you know, I am excited about the administration's proposal to create ARPA-H. It is so promising. You know I have questions about how we avoid duplicating the efforts of existing NIH activities, how we balance investments with ARPA-H, investments in basic research, and how the NIH will make the decisions about what the research is that we pursue. And we want you to make those decisions. You know that this has been a subcommittee that has tried very, very hard not to earmark, if you will, areas of research. That is not our jurisdiction. It really isn't. That is yours.

So excited about the proposals that we know are going forward, and those proposals that are going to look at the health disparities which have been mentioned today, the maternal issues, and so many other critical areas. So I thank the witnesses not just being here today but for the commitment that you have made in your professional careers to focus on how we, in fact, yes, use your talent, your ability, use the NIH to save people's lives. Thank you.

And, with that, I bring this hearing to a close. Thank you.

Material submitted for inclusion in the record follows:

**Committee on Appropriations**  
**Labor, Health & Human Services, and Education Subcommittee**

*FY 2022 Budget Request for the National Institutes of Health*  
*Tuesday, May 25, 2021*

**Questions for the Record**

Dr. Francis S. Collins, Director, National Institutes of Health  
 Dr. Diana W. Bianchi, Director, National Institute of Child Health and Human Development  
 Dr. Anthony S. Fauci, Director, National Institute of Allergy and Infectious Diseases  
 Dr. Gary H. Gibbons, Director, National Heart, Lung, and Blood Institute  
 Dr. Norman E. Sharpless, Director, National Cancer Institute  
 Dr. Nora D. Volkow, Director, National Institute on Drug Abuse

**Submitted by Rep. Lucille Roybal-Allard**

***NIH Use of Non-Animal Research Methods***

After years of assertions by NIH that it was moving towards more inclusion of non-animal methods for research, it was very disappointing to hear you state during the NIH budget hearing that “for the foreseeable future, if we are going to make advances in things like cancer, diabetes, heart disease, rare diseases, we are still going to need to depend for a lot of that effort on animal research.”

There is also a growing awareness of the limitations of the use of animals to accurately model human conditions or to predict human reactions in many areas of research, resulting in serious problems in translation to effective health breakthroughs. Alzheimer’s disease research, one of the proposed areas of interest for ARPA-H, has received major funding for the purpose of modeling the disease in animals, yet over 99% of Alzheimer’s therapeutics that are deemed safe and effective in animals have failed in human clinical trials. Cancer drugs also have a low success rate (only 5% are approved after entering clinical trials) followed by psychiatry drugs (6% success rate), heart drugs (7% success rate) and neurology drugs (8% success rate).

Emerging human biology-based innovations, like organ and tissue chips, organoids, and patient-derived samples, can increase predictiveness of basic biomedical research and nonclinical studies because these methods leverage human biology to produce results that are relevant to humans. The NIH has taken up these methods to some extent, for example through the NCATS Tissue Chip Program, which was partially funded by DARPA; however, despite the biomedical advancements arising from human biology-based innovations, these methods are not prioritized agency-wide.

**Questions:**

1. Has NIH evaluated the return-on-investments for animal-based versus non-animal research projects for the funding it receives?

**NIH Response:**

At the core of its mission, the National Institutes of Health (NIH) funds research to define the nature and behavior of living systems and the application of that knowledge to enhance human health, lengthen life, and reduce illness and disability. NIH is certain that the nation's investment in animal research has been critical for saving countless lives and extending human life expectancy in the United States and around the world. For instance, animal research and testing represented critical steps in the development process for nearly every prescription medicine in our medicine cabinets. Of course, our technological and computing capabilities continue to improve and, as we continue to learn how to replicate and reconstruct complex biological systems, researchers across the world will increasingly utilize a variety of methods in both animal and non-animal systems to conduct vital biomedical research. At this time, although some of these newer methods can complement research, they cannot begin to replace animal models, but NIH will continue to pursue all tools in our arsenal to improve human health.

2. What role has NIH played in educating the research community about non-animal research methods including cell-based methods, computer modeling and simulation, and human tissue studies?

**NIH Response:**

The National Institutes of Health (NIH) provides numerous trainings, programming, and resources to researchers to promote animal care and appropriate use of alternative models. To drive education, NIH works directly with the research community to advance our understanding of the science underlying alternative methodologies, including most recently the 8th Annual 3Rs Symposium: Pandemic-Driven Advances (organized by the Johns Hopkins the Department of Agriculture.)

The NIH also works with the research community to improve the selection, design, and relevance of animal models through a variety of different ways. In 2019, the NIH Director charged the Advisory Committee to the Director (ACD) to make recommendations to enhance the reproducibility and rigor of animal research by improving experimental design, optimizing translational validity, enhancing training, and increasing the transparency of research studies involving animal models. The *ACD Working Group on Enhancing Rigor, Transparency, and Translatability in Animal Research Updates* released its final report in June 2021 ([acd.od.nih.gov/documents/presentations/06112021\\_ACD\\_WorkingGroup\\_FinalReport.pdf](https://acd.od.nih.gov/documents/presentations/06112021_ACD_WorkingGroup_FinalReport.pdf).) The agency is actively evaluating those recommendations and determining strategies for their implementation.

Importantly, NIH has numerous policies and procedures in place to ensure appropriate animal models are selected, including the consideration of non-animal models when appropriate. For one example, as a condition of receiving funding for animal research from NIH, researchers and Institutional Animal Care and Use Committees (IACUCs) are required to ensure that research involving the care and use of animals is reviewed and determined to be scientifically and ethically justifiable with consideration of alternatives. This includes

evaluating the availability or appropriateness of less invasive procedures, other species, isolated organ preparation, cell or tissue-based experiments, or computer simulation in research design. Additionally, NIH intramural researchers must complete an online course regarding animal use every three years, which includes training on replacing, reducing, and refining animal use and consideration of alternatives (such as through searches of the published scientific research literature).

3. Given these less than stellar success rates utilizing animal models, what steps has NIH taken to incentivize researchers to utilize and further develop non-animal research methods?

**NIH Response:**

As mentioned above, research with animal models have yielded countless improvements in human health. The introduction of “New Approach Methodologies” (NAMs) may reduce the use of animals in some types of research studies. The National Institutes of Health (NIH) funds research to support the development of a variety of NAMs including *in vitro* methods (i.e., testing cells and tissues in test tubes or other chambers), 3D tissue culture models, and computational models for predictive toxicology. As an example, NIH-funded research has resulted in the creation of an *in silico* (computer modeling) protocol to predict chemicals that cause skin sensitization and the development and validation of an *in chemico* (chemical reactivity) test for eye irritants to replace animal testing for ocular toxicity. NIH’s Tissue Chip program is supporting the development of bio-engineered devices designed to mimic some functions of the human body; to create predictive models of human response to candidate drug, vaccine, or biologic agent; and to determine whether candidate therapies are safe and effective in humans.

At some point in the future, NAMs may reduce some of the needs for specific animal models, but substantial scientific challenges still remain. While advances in stem cell, organoid, computational, non-invasive imaging, and other technologies are assisting our understanding of complex human systems, research on animals continues to be essential for understanding diseases and developing therapies. Many disease mechanisms cannot be studied in cells or other NAMs because the relevant biology and behavior are simply not present or are too different from human physiology, and thus should be seen as additional tools in our arsenal for preventing, curing, and treating disease, rather than a replacement. When animal models are required, NIH will only conduct and support research in accordance with the highest scientific and ethical principles.

4. How will NIH ensure that each Center for Scientific Review study section includes individuals with expertise in animal-free research methods and that study sections are not primarily composed of those who predominately use animals?

**NIH Response:**

The Center for Scientific Review (CSR) recruits reviewers for study sections based on expertise needed to competently assess the scientific merit of the submitted National Institutes of Health (NIH) grant applications. CSR seeks a diversity in membership, including diversity of scientific perspectives on the science reviewed by the study section. Diversity in scientific perspective includes expertise across a range of methods and model systems.

5. As the Committee considers the Administration's request for a significant investment to launch the ARPA-H, how will you ensure that there is a strategic focus and funding for the development and use of advanced human biology-based research approaches to reach the medical breakthroughs we need?

**NIH Response:**

The Advanced Research Projects Agency for Health (ARPA-H) will provide an entirely new paradigm for biomedical and health research. ARPA-H is envisioned to foster innovative methods, technologies, and broadly applicable platforms to achieve medical breakthroughs that have eluded the current biomedical research ecosystem.

The purpose is to encourage high-risk, high-reward projects in order to transform important areas of medicine and health for the benefit of all patients. Many such ambitious proposals would involve creating platforms, capabilities, and resources that could be applicable across many diseases, which could include the development and use of advanced human biology-based approaches.

***Gynecologic Cancers***

The American Cancer Society's Annual Report to the Nation on the Status of Cancer highlighted that we are making good progress in the battle against cancer, with the incidence and mortality rates for most cancers have dropped significantly. However, among the 20 most common cancers, relative survival for patients significantly improved since the mid-1970s *except for* those with cervical and uterine cancer.

**Question:**

What plans does the NCI have in FY 2022 to develop a paradigm of increased research to improve hope for survival for patients with cervical or uterine cancer?

**NIH Response:**

The National Cancer Institute (NCI) shares the committee's commitment to research on cervical and uterine cancers, including endometrial cancer (cancer of the inner lining of the uterus), and improving outcomes for patients.

NCI is dedicated to eradicating cervical cancer through prevention and early detection. Current human papillomavirus (HPV) vaccines can prevent 90 percent of HPV-related cancers, and NCI continues to support research efforts to increase HPV vaccine uptake and understand vaccine hesitancy. Over half of the new cervical cancer cases in the United States each year are among women who have never been screened or who are infrequently screened, reflecting barriers presented by socioeconomic disparities, geographic inaccessibility, and other factors. NCI has developed the 'Last Mile Initiative' as a public private partnership between federal agencies, industry partners, and professional societies/clinical practice guidelines organizations. This Initiative aims to validate self-sampling-based HPV testing as a comparable alternative to provider-collected cervical specimens for HPV testing in cervical cancer screening. As part of



this Initiative, the NCI will support a nationwide, multicentric screening trial in diverse delivery settings. Self-sampling allows women to obtain specimens for HPV testing in the privacy of their own homes and has significant potential to expand screening to never screened or under-screened women, tackling a pressing public health concern of lack of access to cervical cancer screening. Addressing this challenge will make a critical contribution not only to prevention of cervical cancer by identifying pre-cancerous lesions, but also ensuring invasive cervical cancers are diagnosed at the earliest stage possible, when they are most treatable. Localized (early stage) cervical cancer has a five-year survival rate of 92 percent, further illustrating the importance of early detection in improving survival and overall outcomes for women with cervical cancer.

NCI also supports research to advance our understanding of how to prevent, detect, and treat uterine cancers (endometrial cancer and uterine sarcoma). For example, the Epidemiology of Endometrial Cancer Consortium (E2C2) is an NCI-supported consortium dedicated to studying the etiology of endometrial cancer through collaboration among investigators. Investigators from NCI's Early Detection Research Network designed the PapSEEK test for early detection of endometrial cancers. This test is a type of liquid biopsy that identifies cancer-related alterations in DNA obtained from fluids collected during a routine Pap test to detect some endometrial cancers at earlier, more treatable stages. Similarly, the DETECT (Discovery and Evaluation of Testing for Endometrial Cancer in Tampons) Study is developing ways to detect endometrial cancer in samples of uterine tissue collected using tampons<sup>1</sup>. By comparing uterine tissue from women who are having a hysterectomy for endometrial cancer with tissue from women having a hysterectomy for an unrelated benign condition, scientists in NCI's intramural research program hope to find biomarkers that may eventually lead to noninvasive early detection approaches.

Today, nearly 40 percent of adults are obese, and without intervention, the obesity epidemic will result in more cancers. Uterine cancer incidence and mortality have increased in recent years, believed to be partially associated with rising rates of obesity. Women who are obese or overweight are approximately two to four times as likely as normal weight women to develop uterine cancer, including endometrial cancer, making interventions to address weight and obesity vital to combatting uterine cancer incidence and mortality. Examples of NCI-supported research on this topic include a study of how changes in body composition following weight loss impact inflammatory biomarkers in biopsy-collected endometrial tissue and blood samples and whether these processes differ between Black and White women<sup>2</sup>; the development of a weight loss intervention among Appalachian residents<sup>3</sup>; and a study of the Deep South Interactive Voice Response (IVR)-supported Active Lifestyle (DIAL) Intervention to increase physical activity levels among residents of the Deep South.<sup>4</sup> Additionally, researchers at the University of North Carolina Lineberger Comprehensive Cancer Center are directly examining the metabolic and molecular differences of endometrial tumors in obese and non-obese women. This research team

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<sup>1</sup> [clinicaltrials.gov/ct2/show/NCT03538665](https://clinicaltrials.gov/ct2/show/NCT03538665)

<sup>2</sup> [reporter.nih.gov/search/xJa2HzHYoUqVHmoJf-IrJg/project-details/10129305](https://reporter.nih.gov/search/xJa2HzHYoUqVHmoJf-IrJg/project-details/10129305)

<sup>3</sup> [reporter.nih.gov/search/r8dmLhFhPkiPFcCpLj8sjQ/project-details/10065366](https://reporter.nih.gov/search/r8dmLhFhPkiPFcCpLj8sjQ/project-details/10065366)

<sup>4</sup> [reporter.nih.gov/search/qm18xt\\_1H0CVB8QGj6H8lQ/project-details/10163139](https://reporter.nih.gov/search/qm18xt_1H0CVB8QGj6H8lQ/project-details/10163139)

is also exploring how metformin, widely used to treat type II diabetes, may also exhibit anti-tumor activity through its effects on a patient's metabolism<sup>5</sup>.

The Specialized Programs of Research Excellence (SPOREs), a key component of NCI's Translational Research Program, support research on these cancers including one cervical cancer SPORE and one endometrial cancer SPORE. Translational research to bridge the gap between basic research on cervical and uterine cancers and potential therapies is also essential to improving outcomes for patients. NCI has also been funding planning grants for future SPORE programs in cancer health disparities. The aim is to build programs to improve the prevention, early detection, diagnosis, and treatment of cancers that disproportionately affect specific racial and ethnic minority populations that can compete for SPORE funding in future years. In fiscal year (FY) 2020, Northwestern University in Chicago was awarded a SPORE planning grant focusing on racial differences in gynecologic cancers<sup>6</sup>.

As of May 2021, NCI is supporting over 30 clinical trials with a primary focus on cervical cancer. Examples of these studies include a trial evaluating the use of a novel anti-cancer agent, triapine, in combination with chemotherapy and radiation<sup>7</sup> and a trial studying the use of anti-cancer vaccines to treat cervical cancer<sup>8</sup>. In addition, NCI is supporting over 80 clinical trials with a primary focus on uterine (including endometrial) cancer. Examples of these projects include studies of the use of an immunotherapy agent, in combination with other cancer therapies, to treat high risk endometrial cancer<sup>9</sup>; a trial examining a combination therapy to treat endometrial cancers that express the HER2 protein<sup>10</sup>; and a study evaluating the use of the experimental therapy triapine to treat endometrial serous adenocarcinoma, a difficult to treat subtype of uterine cancer<sup>11</sup>. Clinical trials are an integral part of advancing research in this important topic area, and NCI is committed to reaching out to disparate, at-risk communities to explain, educate, and encourage clinical trial participation.

### ***Overactive Bladder***

Overactive bladder is a devastating condition which affects 38 million Americans and 1 in every 3 older adults. Recent studies on anticholinergic medications, which are commonly prescribed drugs to treat overactive bladder, have shown that these medications have a negative impact on cognition and may lead to the development of Alzheimer's disease and related dementias.

### **Question:**

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<sup>5</sup> [reporter.nih.gov/search/4gpAUqMNRkOH--hySrfDog/project-details/10104456](https://reporter.nih.gov/search/4gpAUqMNRkOH--hySrfDog/project-details/10104456)

<sup>6</sup> [reporter.nih.gov/project-details/9961257](https://reporter.nih.gov/project-details/9961257)

<sup>7</sup> [clinicaltrials.gov/ct2/show/NCT02466971/](https://clinicaltrials.gov/ct2/show/NCT02466971/)

<sup>8</sup> [clinicaltrials.gov/ct2/show/NCT02405221/](https://clinicaltrials.gov/ct2/show/NCT02405221/) and [clinicaltrials.gov/ct2/show/NCT04580771/](https://clinicaltrials.gov/ct2/show/NCT04580771/)

<sup>9</sup> [clinicaltrials.gov/ct2/show/NCT04580771/](https://clinicaltrials.gov/ct2/show/NCT04580771/) and [clinicaltrials.gov/ct2/show/NCT03914612](https://clinicaltrials.gov/ct2/show/NCT03914612)

<sup>10</sup> [clinicaltrials.gov/ct2/show/NCT04585958](https://clinicaltrials.gov/ct2/show/NCT04585958)

<sup>11</sup> [clinicaltrials.gov/ct2/show/NCT04494113](https://clinicaltrials.gov/ct2/show/NCT04494113)

Given the potential adverse impact on the nation's elderly that will only increase as our population ages, is the NIH/NIA studying or have plans to study the association between anticholinergic medications used to treat overactive bladder and cognitive decline in FY 2022?

**NIH Response:**

The National Institute on Aging (NIA) supports studies on a range of issues related to the causes, prevention, and treatment of overactive bladder. This includes research on the safety of long-term use of anticholinergic medications commonly prescribed to treat overactive bladder and the associated risk of cognitive impairment and dementia as well as research to advance safe and effective alternative treatments for overactive bladder.

NIA is currently supporting several studies on the safety of long-term use of anticholinergic medications and the risk of cognitive impairment and dementia in older adults with overactive bladder. This includes a clinical trial testing whether discontinuing use of anticholinergics improves cognition and lowers the risk of Alzheimer's disease and Alzheimer's disease-related dementias. NIA is also funding a clinical trial to test a mobile app that integrates a personalized anticholinergic risk calculator, targeted multimedia such as videos and blogs to educate users regarding anticholinergics, and a conversation starter to help a patient self-initiate ending his/her anticholinergic prescriptions in collaboration with a healthcare provider. This trial will explore the impact of the app on prescription anticholinergic exposure among older adults and on cognitive function and quality of life. Other research studies currently funded by NIA seek to evaluate adverse outcomes of anticholinergic medicines in people living with dementia and overactive bladder; assess severe adverse events associated with the interaction of cholinesterase inhibitors used to treat Alzheimer's disease with anticholinergic medications; test mechanisms of neurotoxicity from anticholinergics; and improve how older adults living with dementia, their caregivers, and clinicians make decisions about using anticholinergic medicines. In addition, a recent NIA-supported study found that exposure to strong anticholinergics increased the risk of transitioning from normal cognition to mild cognitive impairment. NIA is committed to continuing to fund research to improve the lives of people living with overactive bladder and will continue to fund research toward prevention of cognitive impairment.

***Pelvic Organ Prolapse***

Pelvic Organ Prolapse (POP) is a common problem, with 1 out of 8 women undergoing surgery for prolapse in their lifetime. One in three women who has given birth has pelvic organ prolapse. Treatment of pelvic organ prolapse requires significant health care resources; the annual cost of ambulatory care of pelvic floor disorders in the United States from 2005 to 2006 was almost \$300 million. Surgical repair of prolapse is performed twice as commonly as incontinence surgery and constitutes the most common inpatient procedure performed in women older than 70 years.

**Question:**

What research activities is the NICHD planning to initiate in FY 2022 to address prevention of and new treatments for Pelvic Organ Prolapse?

**NIH Response:**

Pelvic floor disorders, including pelvic organ prolapse, are a common problem for women that the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) is working to address. The majority of NICHD sponsored research on pelvic organ prolapse is through the Pelvic Floor Disorders Network (PFDN), a multi-center network that was established by the NICHD in 2001 in response to an increasing awareness by the public and by health professionals of the need for more evidence-based data to guide both surgical and non-surgical care for this large and growing clinical problem. The overall objective of the PFDN is to facilitate interactions between a network of academic centers with the recruitment capabilities and research expertise needed to perform studies that will provide efficient, high quality, evidence-based clinical answers to both providers and women. Studies include both careful analysis of standard treatment outcomes as well as testing new therapies and approaches to move the research agenda forward in novel directions for clinical benefit. For example, PFDN research over the past year has demonstrated that:

- at five years follow up, vaginal mesh used to lift the uterus proves superior to native tissue repair for the surgical treatment of pelvic organ prolapse;
- pain with sexual activity improves after surgical treatment of pelvic organ prolapse;
- the ability to fabricate support tissue from vaginal biopsies of the patient could be incorporated into surgical repairs;
- further identification of risk factors for failure of pelvic organ prolapse surgery based on patient characteristics and magnetic resonance imaging (MRI) findings is feasible; and
- current definitions of success or failure may result in the overestimation of surgical failure rates following pelvic organ prolapse, potentially explaining, in part, the low retreatment rates after pelvic organ prolapse surgery.

NICHD will continue to support this important research in FY 2022. In the fall of calendar year 2021, NICHD plans to issue a funding announcement to renew the PFDN for an additional five years. NICHD will also continue to fund investigator-initiated research on pelvic organ prolapse.

***Health Disparities in Cardiovascular Disease***

Cardiovascular disease exacts a disproportionate toll on racial and ethnic minorities especially African Americans. According to the American Heart Association, cardiovascular disease mortality rates are nearly 34% higher for blacks than the overall U.S. population. The incidence of high blood pressure - a leading risk factor for heart disease and stroke, is also among the highest in the world for African Americans. The prevalence of hypertension among black men is 57.6% and 53.2% among black women.

**Questions:**

1. In your FY 2022 budget, has the NHLBI committed to strengthening its investment in the Jackson Heart Study, the nation's largest study of cardiovascular disease in African Americans.

**NIH Response:**

The National Heart, Lung, and Blood Institute (NHLBI) is committed to strengthening the Jackson Heart Study (JHS) and other studies to address cardiovascular disease disparities. The JHS, which started in 1998 as a collaborative effort among three Jackson-area academic centers, is jointly funded by the NHLBI and the National Institute on Minority Health and Health Disparities (NIMHD). In 2018, NHLBI extended funding for JHS through fiscal year 2024. The University of Mississippi Medical Center (UMMC) serves as the study Coordinating Center; in addition, UMMC, Jackson State University, and Tougaloo College each administer a graduate Training and Education Center (TEC). The Mississippi State Department of Health now administers the study's Community Engagement Center (CEC), leveraging the previous work of the Jackson State University CEC to disseminate cardiovascular health promotion and prevention messages and conduct community-based research.

2. With the planned extension of this study, what has already been discovered about the disproportionate burden of cardiovascular disease on African Americans since this study was first initiated in 1998 and what do investigators hope to discover in the future?

**NIH Response:**

Despite progress in reducing the burden of cardiovascular disease in the United States, racial and geographic disparities persist, and heart disease risk factors including obesity and hypertension have been trending upward and at younger ages. Over the decades, researchers have gained critical insights into factors that influence rates of heart disease in the National Heart, Lung, and Blood Institute (NHLBI)-supported Jackson Heart Study (JHS) cohort and other communities. Among the most powerful factors are health-related behaviors, such as physical activity, diet, and adherence to medications, especially for hypertension. JHS has found that even small spikes in blood pressure are associated with a higher risk of death from heart disease. Social determinants of health also play a significant role, and may interact with behavioral factors; for example, low access to healthcare, low health literacy, and racial bias by healthcare providers can reduce medication adherence. These findings are important for public health education efforts and could lead to new ways for researchers to treat heart disease in African Americans.

Smoking is another significant heart disease risk factor. In 2020, JHS researchers found that African Americans who smoke are nearly 2.5 times more likely to have a stroke than those who never smoked. However, those who quit had a lower risk about the same as never-smokers ([www.ahajournals.org/doi/10.1161/JAHA.119.014990](http://www.ahajournals.org/doi/10.1161/JAHA.119.014990)). The findings suggests that even after years of smoking, African Americans—who as a group are twice as likely as Whites to have a fatal stroke—could significantly reduce their risk by quitting.

JHS also addresses disparities affecting African Americans through community engagement and scientific training programs. The JHS Community Engagement Center (CEC) is translating 20 years of findings into better community health by weaving health education and screenings into daily life and finding innovative ways to reach people at home and in community spaces. For example, its Brothers Reaching Out to Help Educate on Routine Screenings (BROTHERS) program is training barbers to provide blood pressure monitoring and counseling.

The JHS Scholars program provides a pathway to increase the representation of African Americans in the biomedical workforce and has supported more than 100 students from JHS partner institutions. The JHS is also a linchpin of the NIH Community Engagement Alliance (CEAL) Against COVID-19 Disparities initiative, which brings together researchers and local organizations to reach people in the hardest hit communities, ensure their inclusion in vaccine trials, and encourage vaccination. During the pandemic, many JHS scholars became ambassadors in their communities to help fight misinformation and build trust around vaccines.

Looking to future research directions and discovery, the JHS now includes assessments of cognitive function to investigate links between cardiovascular disease and brain health including risks for vascular dementia and cognitive impairment, and the study is one of the cohorts in NHLBI's Trans-Omics for Precision Medicine (TOPMed) program. This program is analyzing genomic and other data for clues to a variety of heart, lung, blood, and sleep disorders—and has assembled one of the world's largest, most diverse genomic databanks.

### ***Cardiovascular Disease in Pregnancy***

The U.S. maternal mortality rate is the worst among industrialized nations, with Black women experiencing disproportionately high rates of pregnancy-related death. Heart disease is the number one medical reason for maternal mortality. Further, many women who experience conditions like preeclampsia or gestational diabetes are at greater risk for heart disease later in life.

#### **Question:**

How is the NHBLI addressing maternal health in its research to protect women's heart health before, during, and after pregnancy?

#### **NIH Response:**

Given that cardiovascular disease is the leading cause of pregnancy-related deaths, the National Heart, Lung, and Blood Institute (NHLBI) has taken a lead role in research to reduce the Nation's alarming rates of maternal mortality and morbidity. NHLBI's research programs in this area take a life-course approach that focuses on improving women's heart health before, during, and after reproductive age. With rising rates of cardiovascular risk factors—such as hypertension, obesity, and diabetes—among girls and young women, many women are entering

their pregnancies at high risk of heart disease, which can result in poor outcomes for the mother and child.

Significant racial and ethnic disparities in maternal morbidity and mortality exist in the United States. Black women are three times more likely to die from a pregnancy-related cause than White women. Over the past decade, pre-pregnancy hypertension among women aged 15-44 nearly doubled, with the highest rates among Black women. NHLBI's Chronic Hypertension and Pregnancy (CHAP) trial is examining the safety and effectiveness of using medication to treat mild chronic hypertension in pregnancy, which is typically deferred for severe hypertension. The Institute also has committed funding through 2027 for the nuMOM2b Heart Health Study, which is examining how pregnancy impacts a woman's future cardiovascular health in a large diverse cohort of new mothers. The study has found that women who experience adverse pregnancy outcomes have worse cardiovascular outcomes, including higher risk for hypertension, as late as 2-7 years after delivery ([pubmed.ncbi.nlm.nih.gov/33619977/](https://pubmed.ncbi.nlm.nih.gov/33619977/)).

NHLBI is also using implementation science to focus on evidence-based interventions that are proven to support maternal health and move them into broader practice. For example, NHLBI's new Maternal Health Community Implementation Program (MH-CIP) will fund several regional coalitions to pilot-test community-based implementation strategies in areas where maternal death rates are high, particularly in the southeast. This will be coupled with other ongoing NHLBI efforts to address other regional health disparities. Additionally, NHLBI's new Early Intervention to Promote Cardiovascular Health of Mothers and Children (ENRICH) will tap into existing federal home health and wellness visiting programs that serve at-risk families to determine if adding heart-healthy lifestyle interventions will enhance maternal and early childhood outcomes. Approximately 3,000 mother-child pairs across various sites will be reached as part of this effort.

### ***Maternal Mental Health Research***

Perinatal mood and anxiety disorders (PMADs) are estimated to affect 1 in 7 pregnant and postpartum women, and a study by Mathematica found that the estimated total societal cost of untreated PMADs in the U.S. was \$14.2 billion for all births in 2017 when following the mother-child pair from pregnancy through five years postpartum. Even when diagnosed, half of perinatal women diagnosed with depression do not get the treatment they need. The COVID-19 pandemic has exacerbated this issue.

#### **Questions:**

1. Please report on the number and description of research grants awarded over the past three fiscal years on women's health innovations that address these PMAD issues?

#### **NIH Response:**

The National Institutes of Health (NIH) supports interdisciplinary research to improve the understanding and treatment of mental illnesses in women, including perinatal mood and anxiety disorders (PMADs). These efforts lay the groundwork for interventions to improve mental health outcomes for women from diverse socioeconomic, racial, ethnic, and

geographic backgrounds in a variety of treatment settings. As an example of recent progress through research in this area, in 2019 the U.S. Food and Drug Administration (FDA) approved brexanolone, the first drug specifically approved to treat postpartum depression (PPD). This approval was the result of a bench-to-bedside journey that began with basic research in the National Institute of Mental Health (NIMH) Intramural Research Program. One example of the numerous NIH-supported research projects currently focused on PMADs is an NIMH-supported study in which researchers are studying DNA methylation – a chemical mark on DNA that changes its expression – in pregnant women who are at elevated risk for PPD. Findings from this study could help to improve early screening and identify new treatment approaches for PPD. In another NIMH-funded study, researchers are using machine learning to develop a PPD risk prediction model and a clinical decision-making tool. These new tools, if shown to be effective, could lead to substantial improvements in the early detection and effective treatment of PPD. NIMH is also supporting research focused on the effects of the coronavirus disease 2019 (COVID-19) pandemic on perinatal mental and anxiety disorders. For example, one team of researchers is investigating the neurobehavioral effects of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) exposure on mothers and their infants, with the goal of identifying intervention strategies to mitigate any long-term impacts of exposure. Another team of researchers is investigating the impact of the COVID-19 pandemic and racial discrimination on mental health, pregnancy-associated morbidity and maternal mortality, and fear psychophysiology during pregnancy and up to three months postpartum in Black women. Data generated from this study will inform risk stratification approaches and mitigation strategies for marginalized populations.

2. Where the NIH can improve in providing opportunities to improve mental health outcomes for prenatal and postpartum women?

**NIH Response:**

The National Institute of Mental Health (NIMH) is committed to supporting research to identify women at increased risk for perinatal mental illnesses, including postpartum depression, and improving mental health outcomes for these women through research on intervention delivery, particularly for underserved and vulnerable populations. As one example of an opportunity for progress in this area, NIMH recognizes that hybrid effectiveness-intervention clinical trials are needed to better understand how perinatal depression interventions may be effectively delivered by local providers at a large scale, across diverse healthcare and community settings. NIMH recently released a pair of Funding Opportunity Announcements (FOAs), as well as a Notice of Information (NOI), to encourage grant applications in this research area. The purpose of the FOAs is to support both preliminary and larger-scale clinical trials to establish the effectiveness of prevention interventions for perinatal depression and associated mental health outcomes, including anxiety, suicidal ideation, and suicidal behaviors. The NOI encourages mental health researchers to submit applications focused on the prevention and treatment of mental illnesses that occur during the perinatal period.



### ***Chronic Kidney Disease***

Chronic kidney disease affects over 37 million adults in the United States, and approximately 25 percent of Medicare's annual budget is spent on this disease. An additional 80 million Americans are at risk of developing CKD due to diabetes, cardiovascular disease, or family history. Kidney disease also heightens morbidity and mortality with acute infections such as SARS-COV-2 and with chronic diseases such as cancer and cardiovascular diseases. Despite this large impact on our healthcare system, NIH funding for kidney disease has lagged far behind that of NIH overall; between fiscal years 2015 and 2020, funding for NIH rose 37 percent, compared to just 19 percent for kidney research. In 2020, NIH spent less than \$20 per kidney patient on research into kidney disease. As funding has stagnated, life lost to kidney patients through death and disability increased 65% over the last 15 years.

#### **Question:**

Can you explain this inequality in funding and how NIH plans to address it?

#### **NIH Response:**

Chronic kidney diseases (CKD) and their associated risk factors and comorbidities, such as diabetes, obesity, cardiovascular disease, and hypertension, exact enormous personal and economic tolls on the U.S. population. This is especially true for persons from U.S. minority populations disproportionately affected by these diseases. Rising rates of obesity are further exacerbating this burden.

The National Institutes of Health (NIH) itself does not allocate set funding amounts for specific diseases; rather, investigator-initiated research ideas, scientific opportunity, and the outcome of NIH's rigorous peer review process help determine how much of NIH's annual appropriations is spent in a particular area. NIH, with the leadership of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the lead institute at NIH for funding of kidney disease, embraces an integrated approach to CKD research that leverages the NIH investment in several diseases and disorders to improve the health of people with or at risk of CKD. For example, NIH-led clinical trials and other studies showed that carefully controlling blood sugar levels to keep them in a healthy range can help stave off onset or progression of kidney disease in people with diabetes. Current NIH efforts to understand, prevent, and treat obesity and diabetes across the lifespan, from understanding the early influences of the intrauterine environment to identifying effective medical interventions, can be expected to have a similar benefit for the CKD community.

The NIH continues to solicit and support research specific to the kidney and plans to continue ongoing research toward improving early diagnosis, prevention, and treatment of CKD. For example, the NIDDK-supported Kidney Precision Medicine Project is analyzing kidney biopsies from a broad range of people, using cutting-edge technologies to better understand kidney diseases and injury, identify new therapeutic targets, and stimulate development of personalized therapies. The (Re)Building a Kidney consortium is seeking ways to restore failing kidney function after injury or disease. A new NIH-funded consortium will focus on CKD of uncertain etiology, or CKDu, a devastating pattern of disease that does not fit the usual CKD risk profiles

and has so far eluded our understanding. In this new era of coronavirus disease 2019 (COVID-19), the NIH is also supporting and conducting research to understand how infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) influences the development or course of kidney disease. Finally, the NIDDK chairs the statutory Kidney Interagency Coordinating Committee and will continue to use meetings not only to share information but also to find new ways to leverage research activities and funding across the NIH—as well as other member agencies—to benefit people with CKD.

### ***Breast Cancer Reconstruction***

Every year, 280,000 women are diagnosed with breast cancer and approximately 107,000 breast reconstructions are performed. As the incidence of breast cancer continues to grow, so do survival rates, thanks to advancements in treatment. Breast cancer survivors are living longer, but it also means they are living longer with the side effects of their treatments, including post-mastectomy numbness. The importance of breast sensation has been highlighted in mainstream media, unmasking an unappreciated outcome by patients and surgeons. Sensation is a functional component of the breast and when left untreated, can lead to increased mechanical and thermal injuries as well as negatively impacting a woman's quality of life as demonstrated in patient reported outcomes (PRO).

Unfortunately, when it comes to breast reconstruction, disparities exist in women who have received mastectomies after a breast cancer diagnosis. Although rates have improved over time, women of color, as well as women covered by Medicare and Medicaid instead of private insurance, are still less likely to receive reconstruction. Reconstruction can have a significant, positive impact on the quality of life in breast cancer survivors.

#### **Questions:**

1. Has NIH done any research on the reasons for the existing disparities in women choosing breast reconstruction?

#### **NIH Response:**

The National Institutes of Health (NIH) is committed to advancing cancer progress for all patients and eliminating health disparities, including reducing the incidence of more advanced breast cancer, which is more common in non-White women. More advanced cancer complicates breast cancer treatment and may limit if and when women are able to obtain reconstruction. For example, if a patient has a late-stage cancer that requires radiation after a mastectomy, reconstruction may not begin until after her treatment is completed because radiation may increase the risk of wound healing problems or infections in reconstructed breasts. More information on factors clinicians and women may consider regarding reconstruction is available at [www.cancer.gov/types/breast/reconstruction-fact-sheet](http://www.cancer.gov/types/breast/reconstruction-fact-sheet).

For those women for whom reconstruction is a viable clinical choice, several studies in recent years have documented disparities among women who undergo breast reconstruction

following breast cancer therapy. Much of this work has been conducted by researchers at National Cancer Institute (NCI)-Designated Cancer Centers and other NCI-supported research institutions.

In 2017, a group of investigators at several NCI-supported Florida institutions reviewed numerous published studies that consistently reported that African American women are significantly less likely than White women to undergo any type of breast reconstruction.<sup>12</sup> A 2019 systematic review, conducted by researchers at Johns Hopkins Hospital, found that Medicaid beneficiaries were on average less likely to receive breast reconstruction than patients with private insurance<sup>13</sup>. A study published in 2021, in which researchers analyzed data from the University of Cincinnati Medical Center, also indicates that patients are more likely to undergo any type of breast reconstruction if they have private insurance and identify as White<sup>14</sup>. The data also showed that patients who lived closer to this major medical center were more likely to undergo reconstruction than those who lived more than 40 miles away, indicating potential geographic disparities in access to surgeons qualified to perform reconstructive surgery. More recent data suggest that the expansion of Medicaid – first implemented in certain states in 2010 – has helped to reduce, although not eliminate, certain disparities due to low education level and low income<sup>15</sup>.

A research team at the NCI-supported University of California, Los Angeles, looked specifically at immediate breast reconstruction, which is both often preferred by women and less common because of considerations related to disease stage and other treatments. In 2021, they reported that predictors of immediate breast reconstruction included younger age, White race, private insurance, top income quartile, fewer other health conditions, receiving care at an institution designated as a teaching hospital, high mastectomy volume (large amount of tissue removed), and performance of bilateral mastectomy (removal of both breasts). The increasing use of immediate breast reconstructions suggests these disparities may persist.

NCI-Designated Cancer Centers offer highly specialized care and tend to have more robust personnel and other resources than community-based cancer centers, so women's receipt of breast reconstruction may vary in these institutions as compared to other locations. In 2016, NCI-supported researchers at the Siteman Cancer Center at Washington University St. Louis published findings from a study to further investigate breast reconstruction rates and determinants at their institution. They found a breast reconstruction rate of 54 percent for the study sample of 4,154 African American and White women who received mastectomy for definitive breast cancer treatment, much higher than the rates of five to 29 percent reported from community-based studies. Unfortunately, the researchers also reported reconstruction was less likely in women who were aged 55 and older, had public insurance, received unilateral mastectomy, and received adjuvant radiation therapy. African American women were 30 percent less likely to receive breast reconstruction than White women. In response to this study, Siteman Cancer Center has increased its efforts to inform women of available

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<sup>12</sup> [pubmed.ncbi.nlm.nih.gov/28975838/](https://pubmed.ncbi.nlm.nih.gov/28975838/)

<sup>13</sup> [pubmed.ncbi.nlm.nih.gov/31766937/](https://pubmed.ncbi.nlm.nih.gov/31766937/)

<sup>14</sup> [pubmed.ncbi.nlm.nih.gov/33675136/](https://pubmed.ncbi.nlm.nih.gov/33675136/)

<sup>15</sup> [pubmed.ncbi.nlm.nih.gov/34319475/](https://pubmed.ncbi.nlm.nih.gov/34319475/)

financial, social, and other support services to circumvent barriers to receiving breast reconstruction.

To address these well-documented disparities in breast reconstruction and other surgical procedures, NCI and the National Institute on Minority Health and Health Disparities (NIMHD) are supporting research through the funding opportunity announcement (FOA) “Surgical Disparities Research” (PAR-20-079). In recognition that the factors that influence a patient’s decision-making go beyond herself and include clinician and institutional factors, the FOA encourages research that aims to identify multi-level strategies to address surgical disparities.

NIH will continue to support research on the factors that give rise to health disparities to refine the evidence base, used by regulators, insurance carriers, and policymakers, to shape policies for breast reconstruction access.

2. What can NIH do, in its NCI designated comprehensive cancer centers, to eliminate existing disparities regarding reconstruction, as well as increase awareness of advanced technologies that can help women regain sensation?

**NIH Response:**

The National Cancer Institute (NCI) is committed to addressing health disparities across the cancer control spectrum, including those that affect cancer survivors.

NCI supports research and resources to enhance quality of life for women undergoing breast cancer surgery and reconstruction. For example, to ensure that patients are able to make informed decisions surrounding their cancer care, researchers at the University of Texas-Austin supported by NCI as part of the comprehensive cancer centers are developing predictive algorithms and communication mechanisms to enable providers to work with patients to optimize quality of life following breast reconstruction<sup>16</sup>. Other researchers at the University of Texas-Austin, supported by the National Institute of Biomedical Imaging and Bioengineering (NIBIB), are developing a method of assessing a woman’s perception of the current appearance of her torso and how her appearance will be changed by breast cancer treatment<sup>17</sup>.

NCI also provides information on breast cancer treatment, including breast reconstruction<sup>18</sup>, particularly through the Physician Data Query (PDQ), NCI’s cancer information database. The PDQ database contains summaries of the latest published information on cancer prevention, detection, genetics, treatment, supportive care, and complementary and alternative medicine. NCI has also worked with the U.S. Department of Health and Human Services (HHS) Office of Women’s Health and other HHS agencies to provide educational materials about the availability and coverage of breast reconstruction and other available

<sup>16</sup> [reporter.nih.gov/search/QgNEr09ftUKJdeJz58aCqg/project-details/9878066](https://reporter.nih.gov/search/QgNEr09ftUKJdeJz58aCqg/project-details/9878066)

<sup>17</sup> [reporter.nih.gov/search/WRAs-uBsEEmAidEvYttoJg/project-details/10196213](https://reporter.nih.gov/search/WRAs-uBsEEmAidEvYttoJg/project-details/10196213)

<sup>18</sup> [www.cancer.gov/types/breast/reconstruction-fact-sheet](https://www.cancer.gov/types/breast/reconstruction-fact-sheet)

alternatives post-mastectomy, to support HHS OWH in wide dissemination of these resources through its website<sup>19,20</sup>.

NCI-Designated Cancer Centers serve as an essential component of the United States biomedical research infrastructure, conducting basic, translational, prevention, cancer control, population science, clinical, and survivorship research at 71 sites across the country. Fifty-one of these sites are designated as Comprehensive Cancer Centers, in recognition of the depth and breadth of their research portfolios. Addressing cancer-related health disparities is central to the mission of NCI-Designated Cancer Centers, and applications for funding are scored, in part, based on community outreach and engagement efforts. Specifically, the most recent funding opportunity announcement (FOA) states, “Centers are expected to engage communities within their catchment area to decrease their cancer burden, particularly among minority and underrepresented populations. To facilitate these activities, Centers establish community advisory board(s) and partnerships with healthcare delivery systems and state and community agencies for dissemination of evidence-based findings”<sup>21</sup>.

NCI-Designated Cancer Centers will continue to seek to lessen the morbidity and mortality caused by cancer in their communities. Certain NCI-designated centers conduct outreach, engagement, and education efforts in their catchment areas that include a specific focus on breast cancer prevention, treatment, and follow-up services, as well as reducing disparities in access and outcomes (e.g., the Washington University Siteman Cancer Center, the University of Kansas Cancer Center, Stanford University, and NYU Langone’s Perlmutter Cancer Center). For example, in 2016, NCI-supported researchers at the Siteman Cancer Center at Washington University St. Louis published findings from a study to further investigate breast reconstruction rates and determinants at their center<sup>22</sup>. The authors note that NCI-designated centers are specialized institutions with more standardized models of cancer treatment, and typically report higher breast reconstruction rates than primary healthcare facilities. However, it is unclear whether breast reconstruction disparities are reduced for women treated at comprehensive cancer centers, and they aimed to explore that unanswered question at their own center. They found a breast reconstruction rate of 54 percent for the study sample of 4,154 African American and White women who received mastectomy for definitive breast cancer treatment. Women who were aged 55 and older who had public insurance, received unilateral mastectomy, and received adjuvant radiation therapy were significantly less likely to receive breast reconstruction. African American women were 30 percent less likely to receive breast reconstruction than White women.

The NCI Community Oncology Research Program (NCORP) is a national network that brings cancer clinical trials and care delivery studies to people in their communities through a network of community-based sites and more than 1,000 affiliated practices (e.g., hospitals, oncology clinics, etc.) across the country. Through NCORP’s cancer care delivery research

<sup>19</sup> [www.womenshealth.gov/breast-reconstruction-after-mastectomy](http://www.womenshealth.gov/breast-reconstruction-after-mastectomy)

<sup>20</sup> [www.womenshealth.gov/blog/breast-reconstruction](http://www.womenshealth.gov/blog/breast-reconstruction)

<sup>21</sup> [grants.nih.gov/grants/guide/pa-files/par-20-043.html](http://grants.nih.gov/grants/guide/pa-files/par-20-043.html)

<sup>22</sup> [pubmed.ncbi.nlm.nih.gov/27429869/](http://pubmed.ncbi.nlm.nih.gov/27429869/)

efforts, NCI is supporting two active clinical trials focused on women with breast cancer and their decision-making process in partnership with their healthcare team. The first trial, *Increasing Patients' Engagement in Breast Cancer Surgery Decision-Making*, studies how well a breast cancer surgery decision aid works in increasing patient engagement in decision-making for patients with newly diagnosed breast cancer<sup>23</sup>. The trial also examines barriers to patient engagement even with the use of a decision aid, and if barriers are more likely to be experienced by socioeconomically disadvantaged patients. The second trial, *Improving Patient-Centered Communication in Breast Cancer Through Patient and Provider Interventions*, studies the effectiveness of different interventions on patient-reported outcomes of patient-centered communication and decision-making about breast cancer treatment<sup>24</sup>.

NCI will continue to support research through NCI-Designated Cancer Centers, NCORP, and other research programs and projects, to address disparities in cancer care and outcomes and to improve the cancer care decision-making process for all people with cancer, including breast cancer patients.

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<sup>23</sup> [clinicaltrials.gov/ct2/show/NCT03766009](https://clinicaltrials.gov/ct2/show/NCT03766009)

<sup>24</sup> [clinicaltrials.gov/ct2/show/NCT04549571](https://clinicaltrials.gov/ct2/show/NCT04549571)

**Submitted by Rep. Mark Pocan*****ARPA-H Focus on Radiation Oncology***

Question: My question concerns research funding for cancer treatment options, including radiation therapy. I commend the Administration on its dedication to investing in biomedical research through the creation of the Advanced Research Projects Agency for Health (ARPA-H) and am particularly pleased to see an emphasis being placed on cancer.

The federal investment in cancer research has played a role in every major innovation in the fight against cancer, including significant advances in radiation oncology that have allowed physicians to more effectively treat tumors while minimizing side effects. This has led to a decline in the overall number of cancer deaths in the U.S and allowed many more people to live healthy and productive lives.

But we know more can be done to benefit more patients, and applied research through ARPA-H seems like a ripe opportunity to make the next leap forward in radiation treatments. For instance, further exploration of the benefits of combining immunotherapy and radiation therapy and the use of radiopharmaceuticals have tremendous potential. Despite its efficacy, radiotherapy research has been historically underfunded, with its percentage of NCI's budget being in the single digits every year. However, cancer remains the second common most cause of death in the United States.

Given that more than 50% of cancer patients receive radiation therapy as part of their cancer treatment, how can we ensure, and can you commit, that radiation oncology will be a focus of ARPA-H?

**NIH Response:**

The Advanced Research Projects Agency for Health (ARPA-H) would provide a novel pathway to catalyzing transformative health breakthroughs that cannot readily be accomplished through traditional research or commercial activity. It will focus on filling gaps in the biomedical ecosystem to find solutions to problems that have eluded researchers to date. To address cancer as a leading cause of death, ARPA-H would engage with stakeholders to identify key areas of need for improvement in cancer prevention and treatment, which may include radiotherapy research. Thus far, suggestions for cancer projects include research using messenger RNA (mRNA) to teach the immune system to recognize common genetic mutations that drive cancers, so that the body will wipe out cancer cells when they first arise, or new manufacturing processes to create patient-specific T-cells to search and destroy malignant cells to reduce the costs of these therapies.

A key goal of ARPA-H is to build and develop capabilities and platforms that are broadly applicable to a wide range of diseases and conditions. Any innovative approach to solving a difficult challenge that others have not been able to tackle and that has the potential to deliver significant benefits to human health may be considered.

### ***Gynecologic Cancer Research Funding***

Question: Gynecologic cancers are not unique in one way – funding of high impact research is critical to achieving a decrease in incidence and death from gynecologic cancers. Yet, gynecologic cancers are unique in the decline in NCI funding over time and the disproportionately low level of funding when considering the lethality of the cancers. For example, between 2007 and 2014, prostate cancer research received an average of \$1,821,000 per person-years of life lost, while ovarian cancer received \$97,000, cervical cancer \$87,000, and uterine cancer \$57,000.<sup>25</sup> How will NIH/NCI address this disparity in funding in FY 2022?

#### **NIH Response:**

The National Institutes of Health (NIH) and the National Cancer Institute (NCI) is committed to making progress against all cancers, including gynecologic (GYN) cancers, and supports a broad portfolio of ovarian, cervical, and uterine/endometrial cancer research. The NIH, including NCI, does not allocate funding prospectively by disease type or research category. The NIH Research, Condition, and Disease Categorization (RCDC) analysis of Fiscal Year (FY) 2020 showed that NCI and other NIH institutes spent \$304 million on over 650 research projects focused specifically on gynecologic cancers, including ovarian, cervical, vaginal, and uterine cancers. The total is derived from the totals reported for each of these four cancers in the NIH categorical spending website<sup>26</sup>, adjusted for duplication across categories. Of that amount, NCI supported approximately 559 projects, for a total of more than \$249 million.

It is important to clarify that RCDC categories are not budget line items. Each category represents a list of projects selected for funding through the rigorous NIH peer review process and provides a look back at projects funded in a given fiscal year. NIH, including NCI, does not allocate funding proactively by category.

NCI continues to make significant investments in moving GYN cancer research opportunities forward, while at the same time supporting similarly important investments across the breadth of the cancer research portfolio – from basic science to cancer prevention, to research focusing on survivorship and quality of life for all cancer patients. NCI continues to support both pre-clinical projects and clinical trials focused on specific cancer types, including GYN cancers, as well as trials that are disease-agnostic (focused on the molecular characteristics of the tumor rather than the tumor's site in the body), which women with GYN cancers can also enroll in. For example, to date, 1,298 women with GYN cancers have enrolled in the NCI MATCH precision medicine trial, and 113 women with GYN cancers have enrolled in NCI's disease site-agnostic "DART" trial, evaluating a combination of immunotherapies in treating various types and subtypes of rare cancers, including rare GYN cancer subtypes.

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<sup>25</sup> <https://pubmed.ncbi.nlm.nih.gov/30404721/>

<sup>26</sup> [report.nih.gov/categorical\\_spending.aspx](https://report.nih.gov/categorical_spending.aspx)



NCI has a responsibility to encourage and support research on all types of cancer, and does this through a variety of mechanisms, including support for disease-specific steering groups and the convening of scientific meetings and relevant cross-cutting research areas that seek to identify new scientific directions and opportunities. Through these efforts, NCI is a leader in developing and supporting definitive, practice-changing gynecologic (GYN) clinical trials, as well as responding to areas of scientific inquiry that are unaddressed by private industry. The NCI-supported National Clinical Trials Network has a GYN Cancers Steering Committee that sets clinical trials strategic priorities that address areas of unmet clinical need, important unanswered clinical questions, and potential new approaches to disease treatment<sup>27</sup>. The Institute has supported and advanced GYN cancer research that will provide greater insight into these cancers, additional options for drug therapies, and improved surgical techniques with the intent of increasing survivorship and quality of life. As of May 2021, NCI is supporting more than 80 interventional clinical trials with a primary focus on gynecologic cancers. As noted above, NCI also has several trials that are disease agnostic, and available for women with GYN cancers to consider for enrollment.

Further research on GYN cancers is supported through Specialized Programs of Research Excellence (SPORes). These programs include basic and clinical/applied scientists working together to support projects that will result in new and diverse approaches to the prevention, early detection, diagnosis, and treatment of cancer. NCI currently supports six ovarian SPORes located at Dana-Farber Harvard Cancer Institute, Johns Hopkins University, the Mayo Clinic, Northwestern University, Roswell Park Cancer Institute, and University of Texas MD Anderson Cancer Center. NCI also supports a cervical cancer SPOR at Johns Hopkins University, as well as endometrial cancer SPORes at Northwestern University and the University of Texas MD Anderson Cancer Center.

In addition to the research supported through NCI's clinical trials networks and the SPOR program, the Institute supports numerous investigator-initiated research projects with relevance to gynecologic cancer prevention, screening, population science, survivorship, and treatment. Examples of this research include a study to elucidate the relationship between molecular subgroups of endometriosis-associated ovarian cancers to survival and risk<sup>28</sup>; multi-level interventions to improve update of cervical cancer prevention services in Appalachia<sup>29</sup>; and a project aimed at molecularly characterizing tumors from 500 women (250 African American, 250 white) with high grade endometrial cancers<sup>30</sup>. NCI will continue to support and identify opportunities to better understand and address gynecologic cancers.

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<sup>27</sup> [cancer.gov/about-nci/organization/ccct/steering-committees/nctn/gynecologic](https://cancer.gov/about-nci/organization/ccct/steering-committees/nctn/gynecologic)

<sup>28</sup> [maps.cancer.gov/overview/DCCPSGrants/abstract.jsp?applId=10117829&term=CA248288](https://maps.cancer.gov/overview/DCCPSGrants/abstract.jsp?applId=10117829&term=CA248288)

<sup>29</sup> [maps.cancer.gov/overview/DCCPSGrants/abstract.jsp?applId=10310666&term=CA229143](https://maps.cancer.gov/overview/DCCPSGrants/abstract.jsp?applId=10310666&term=CA229143)

<sup>30</sup> [maps.cancer.gov/overview/DCCPSGrants/abstract.jsp?applId=9916725&term=CA200864](https://maps.cancer.gov/overview/DCCPSGrants/abstract.jsp?applId=9916725&term=CA200864)

**Submitted by Rep. Katherine Clark*****Framingham Heart Study*****Questions:**

Dr. Gibbons -- Many NIH-funded projects that were not directly related to COVID-19 have been disrupted as a result of this pandemic. This was particularly apparent in large-scale longitudinal research projects like the historic Framingham Heart Study. The Framingham Heart Study has benefitted from the NIH's long history of investment, but it is now at risk due to the pandemic and shifting resources. What is the National Heart, Lung, and Blood Institute's plan for protecting projects like the Framingham Heart Study?

**NIH Response:**

The coronavirus disease 2019 (COVID-19) pandemic has impacted all biomedical research including the Framingham Heart Study (FHS), which has been continuously funded by the National Institutes of Health (NIH) since 1948. First and foremost, NIH is committed to the safety and welfare of research staff and participants. However, we also recognize that research is often personal and hands-on by necessity, whether it focuses on people, cells, or molecules. When the COVID-19 public health emergency was first declared, NIH, worked with other Federal entities, including the Office of Management and Budget and the Department of Health and Human Services, to quickly identify flexibilities to protect time-sensitive funding and resources for research and the research community. Those flexibilities included extensions of study reporting timelines, funding extensions, and administrative supplements for unanticipated study costs arising from the pandemic, such as temporary laboratory and clinic closures.

A unique issue with longitudinal population health studies such as FHS is that such studies involve serial clinical exams of the participants. The FHS includes two major cohorts that were going through exams in 2019-2021, which were delayed by the pandemic, creating a domino effect and the need to fund both missed exams and future exams.

Fortunately, FHS investigators and NIH staff have significant expertise in longitudinal research and were well positioned to recoup study time due to the pandemic. The National Heart, Lung, and Blood Institute (NHLBI) worked with FHS principal investigators to develop a mitigation strategy to shield the study and ensure continuation of essential research program functions. For example, researchers were exempted from meeting some of the study's short-term progress milestones and new milestone schedules were developed.

NIH recognizes that the effects of COVID-19 may affect the ability of patients and other volunteers to participate in a variety of NIH-funded research programs, including clinical trials. To maintain support for NHLBI-funded clinical trials impacted by the pandemic, the Institute's program officers worked closely with principal investigators to implement Corrective Action Plans for trials that were unable to meet patient recruitment milestones and to adjust schedules for phased clinical trial awards transitions. Finally, many NHLBI-funded cohort studies and clinical trial networks received supplemental funding to join collaborative NIH and NHLBI-

funded programs created to address the pandemic, including the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) initiative and the Community Engagement Alliance (CEAL) Against COVID-19 Disparities.

### ***Framingham Heart Study***

#### **Questions:**

Drs. Collins and Gibbons -- Congress successfully passed \$4.9 billion in supplemental NIH funding to support research and development on COVID-19. Are there additional resources that the agency needs to ensure that projects like the Framingham Heart Study are protected from disruption?

#### **NIH Response:**

Steady, sustained funding for the Framingham Heart Study (FHS) infrastructure and research activities has helped ensure the study's continued productivity, even during the coronavirus disease 2019 (COVID-19) pandemic. To make up for time lost due to the pandemic, the National Heart, Lung, and Blood Institute (NHLBI) recalibrated study resources, with funds planned that had been designated for the next round of exams re-designated to the current round of exams. NHLBI staff and principal investigators continue to work together to resolve pandemic-related issues and delays.

**Submitted by Rep. Cheri Bustos**

***Down Syndrome***

Question: What has the NIH learned about the linkages between Down syndrome, auto-immunity, and the COVID-19 virus that makes people with an extra copy of chromosome 21 more vulnerable and is NIH pursuing research that could help individuals with Down syndrome and typical individuals at risk for COVID-19 and other current and new pathogens?

**NIH Response:**

The National Institutes of Health (NIH) has made significant investments in understanding Down syndrome, through the INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndrome (INCLUDE) Project. INCLUDE released a Notice of Special Interest (NOSI) in June 2020 specifically dedicated to better understanding the pathology, prevention, diagnosis, sequelae, and treatment of coronavirus disease 2019 (COVID-19) in people with Down syndrome and, as of May 2021, has funded three supplements under this program. One of the studies is designed to explore the interferon response, which is part of the altered immune system in people with Down syndrome that contributes to autoimmunity in these individuals. These studies will shed light on how the immune response to COVID-19 infection in people with Down syndrome impacts their disease course, including the fact that they are more likely to be hospitalized, develop secondary bacterial infections, and die at younger age from the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. Another study is examining the methylation pattern that may reflect the biological, genetic, and epigenetic factors that influence the response to SARS-CoV-2 in people with Down syndrome. Finally, another study is designed to examine the impact of COVID-19 on the mental health of people with Down syndrome and their caregivers through surveys and evaluations, as well as study biological markers of stressful life events and mental health in these individuals.

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) is supporting additional research in this space. Several research teams at the NICHD-funded Eunice Kennedy Shriver Intellectual & Developmental Disabilities Research Centers (EKS-IDDRC) Network have expanded their programs to include COVID-19 projects. NICHD manages the Safe Return to School Diagnostic Testing Initiative, part of the NIH Rapid Acceleration of Diagnostics-Underserved Populations (RADx-UP) program, to promote the safe return to school for children with intellectual and developmental disabilities (IDD), including Down syndrome. These programs are studying COVID-19 testing and mitigation efforts in children and staff within a variety of school settings that serve individuals with IDD. Because children with IDD are at dramatically higher risk of becoming infected, experiencing severe illness or death from COVID-19, and are vulnerable to the negative impact of school closure, given the devastating impacts of the pandemic on access to school-based therapies and other educational resources, these studies will help identify strategies to ensure children with IDs can safely return to school.

**Submitted by Rep. Brenda L. Lawrence**

***Subject: Health Disparities***

I represent a majority-minority district in southeast Michigan, and the past year has exposed the alarming disparities for communities of color. I believe it is absolutely critical that we act on these disparities, develop plans, and invest research dollars in an effort to eliminate these disparities in the future.

Question 1: Dr. Collins, how will the NIH—particularly the National Institute on Minority Health and Health Disparities—combat disparities like those exposed by COVID-19 to ensure we as a country are better prepared in the future?

**NIH Response:**

Long-standing systemic health and social inequities have put many people from racial and ethnic minority groups at increased risk of severe coronavirus disease 2019 (COVID-19) disease. Inequities in the social determinants of health, such as housing, access to healthy foods, economic and educational opportunities, occupation, and access to internet, increase the risk of racial and ethnic minority groups being infected with COVID-19 as daily exposure to people is more common and sheltering in place is more challenging. In addition, healthcare access reflected by lower health insurance coverage or Medicaid coverage instead of private insurance leads to barriers in utilization and delays in obtaining care that may result in higher risk of getting sick and dying from COVID-19.

To provide trustworthy, science-based information to communities most impacted by the COVID-19 pandemic, the National Institutes of Health (NIH) established the Community Engagement Alliance (CEAL) Against COVID-19 Disparities initiative ([covid19community.nih.gov/](https://covid19community.nih.gov/)) led by the National Institute on Minority Health and Health Disparities (NIMHD) and the National Heart, Lung, and Blood Institute (NHLBI). CEAL supports inclusive participation in research through engagement, outreach, and education focused on correcting misinformation about COVID-19 and addressing mistrust in science and the research process. These efforts focus on populations hardest hit by the COVID-19 pandemic, including African Americans, Hispanics/Latinos, American Indian/Alaska Natives, Asian Americans, Native Hawaiians, and Pacific Islanders, with the goal of building sustainable and enduring partnerships. An essential lesson learned is the importance of engaging trusted community-based organizations and leaders to serve as champions who disseminate information about the importance of participating in COVID-19 research. CEAL also has pivoted to address vaccine hesitancy by communicating data on the safety and efficacy of the COVID-19 vaccines and promotion of vaccine uptake. CEAL's website is available in English and Spanish, contains resources for researchers, clinicians, community health workers, and others interacting with community members that can be disseminated widely and customized to fit the needs of specific communities. CEAL has created a model for activating a coordinated community-engaged response in full partnership with academic researchers, public health departments and NIH for meeting the ongoing challenges of the COVID-19 pandemic and future emergencies as well as ongoing chronic diseases that contribute to existing health disparities.

Furthermore, in response to the disproportionate impact of COVID-19 on racial and ethnic minority groups, and other vulnerable communities including rural populations, NIH established the Rapid Acceleration of Diagnostics for Underserved Populations (RADx-UP) initiative with supplemental appropriations in 2020. The overarching goals of the RADx-UP initiative are to: understand the factors associated with disparities in COVID-19 morbidity and mortality and to lay the foundation to reduce disparities for those underserved and vulnerable populations more impacted by COVID-19 disease; enhance COVID-19 testing among underserved and vulnerable populations across the United States; strengthen the available data on disparities in infection rates, disease progression and outcomes; and identify strategies and interventions to reduce these disparities in COVID-19 diagnostics. RADx-UP is focused on promotion of testing for COVID-19 in underserved populations and is now in 33 states, the District of Columbia, and Puerto Rico.

NIMHD led a request for proposals to promote COVID-19 vaccine uptake in a rapid cycle and this effort led to funding seven R01 grants to include community-engaged interventions, targeted interventions for underserved populations, and healthcare system-based interventions. NIMHD in partnership with other NIH Institutes and Offices has co-led efforts to address the social, behavioral, and economic consequences associated with COVID-19 pandemic as this affects populations with health disparities. These efforts have led to the funding of nearly 30 grants targeting specific disadvantaged groups.

In addition, the NIH Minority Health and Health Disparities Strategic Plan represents a commitment by NIH to support research aimed at addressing the risk and protective factors that operate and interact on multiple levels to impact the well-being of populations. To ensure the appropriate representation of minority and other populations with health disparities in NIH-funded research, sustaining goals and specific strategies include: providing guidance, recommendations, and technical assistance for NIH-funded researchers in appropriate study design and best practices for recruitment to ensure compliance with laws, regulations, and policies regarding the inclusion of minorities and other populations with health disparities in research; promoting and enforcing accountability for inclusion of diverse populations by tracking of originally proposed recruitment strategies and objectives to ensure sufficient samples for analyses of sub-population data; and promoting inclusion of minorities and other populations that experience health disparities in big data sets, clinical research, and future big science initiatives.

Lastly, NIMHD is leading the advancement of the science of minority health and health disparities in several ways. The NIMHD Research Framework is a model that depicts a wide array of health determinants relevant to understanding and addressing minority health and health disparities and promoting health equity. NIMHD is supporting community and digital healthcare interventions to advance research to understand the social, behavioral, and economic health impacts associated with COVID-19-related disparities among racial and ethnic minorities and other vulnerable groups. NIMHD also supports research that advances the understanding, prevention, and reduction of pregnancy-related complications and death among racial and ethnic minority women and socioeconomically disadvantaged women, including those in rural settings. In addition, NIMHD supports cutting-edge interdisciplinary research focused on examining pathways and mechanisms through which social factors and social environments might alter gene expression and contribute to health disparities in different populations. NIMHD is also leading a

new NIH-wide effort to advance the scientific study of the role of structural racism and discrimination in causing and sustaining health disparities and to test solutions to address these factors to improve health and reduce health disparities.

Question 2: Dr. Fauci, in your role as Director of the NIAID, what lessons have we learned that can help guide future responses—especially relating to health disparities?

**NIH Response:**

Coronavirus disease 2019 (COVID-19) is a global infectious disease pandemic that has required an unprecedented public-private research effort. The National Institute of Allergy and Infectious Diseases (NIAID) recognizes that Americans in underserved and minority communities have been disproportionately affected by this pandemic, as is the case for some other infectious diseases as well. NIAID is committed to continuing to work directly with these communities and partnering with other Federal agencies and with industry and academia to ensure that no one in vulnerable communities is left behind as we move forward towards defeating the COVID-19 pandemic and addressing health disparities in future biomedical research responses.

NIAID utilized its existing domestic and international clinical trials infrastructure, originally established to conduct research on HIV and influenza, and worked with partners in the public and private sectors to establish the COVID-19 Prevention Network (CoVPN). The CoVPN has supported multiple COVID-19 vaccine candidates to progress in record time from concept to authorization for emergency use by the U.S. Food and Drug Administration (FDA). The CoVPN developed an extensive community engagement framework to reach out to the underserved and minority communities disproportionately affected by COVID-19; to better understand their interest in, and concerns about, research participation; and to partner with them to ensure that their vital input is reflected in the conduct of these clinical studies.

To further address the critical challenges of participation in clinical trials as well as vaccine acceptance and vaccine hesitancy, the National Institutes of Health (NIH) established the Community Engagement Alliance Against COVID-19 Disparities (CEAL) initiative, led by the National Heart, Lung, and Blood Institute (NHLBI) and the National Institute on Minority Health and Health Disparities (NIMHD). CEAL brings together trusted community leaders to serve as champions who share information about the importance of participating in COVID-19 research and communicate data on the safety and efficacy of authorized COVID-19 vaccines. NIH also supports the Rapid Acceleration of Diagnostics (RADx<sup>SM</sup>) Underserved Populations (RADx-UP<sup>SM</sup>) initiative for community-engaged research focused on increasing access to and uptake of COVID-19 testing in underserved and COVID-19 vulnerable communities across the country and understanding and addressing the barriers to COVID-19 testing. RADx-UP also is developing strategies to reduce disparities in COVID-19 testing by supporting projects across the country with established community partnerships. NIMHD is administering the RADx-UP Coordination and Data Collection Center, a national resource to coordinate and facilitate research funded through RADx-UP grants.

In addition, NIH worked with trial sponsors to prioritize the inclusion of populations at greater risk for infection and serious disease, including minority communities, in Phase III clinical trials of NIH-funded COVID-19 vaccine candidates. Generating a diverse group of participants was a major focus of recruitment and community engagement activities coordinated and overseen by NIAID and partners in the public and private sectors. NIAID applied novel real-time data tracking tools and outbreak data analytics to inform trial design, site selection, and recruitment of at-risk individuals. These tools enabled more effective recruitment of diverse populations, which helped to ensure that the COVID-19 vaccines were safe and effective across populations.

The COVID-19 pandemic has highlighted the importance of working with leaders in underserved and minority communities to engage with these communities, understand any hesitations they may have about participating in clinical trials, address their concerns, and ensure they are represented in research to develop medical countermeasures against infectious diseases. Using lessons learned from the COVID-19 pandemic, NIAID will continue to build on the relationships that have been expanded in underserved and minority communities and is committed to continue listening to these communities as we conduct and support research to confront present and future infectious disease threats.

***Subject: COVID Disparities***

Earlier this month, members of the Congressional Black Caucus hosted a Mass Vaccination Week in an effort to get more people vaccinated. One of the biggest concerns I have is the ongoing difficulty overcoming vaccine hesitancy—especially in minority communities. Dr. Fauci, at the end of February, you joined a CBC town hall to discuss myths relating to the COVID-19 pandemic.

Question 1: Dr. Fauci, with some of these same concerns still prevalent in our communities, what advice would you give to people who are still hesitant to get the vaccine? What more do you think can be done to really highlight the need to get vaccinated?

**NIH Response:**

It is critical that we continue to vaccinate as many people as we can, as quickly as possible. U.S. Food and Drug Administration (FDA)-authorized and FDA-approved coronavirus disease 2019 (COVID-19) vaccines meet FDA's rigorous standards for safety and efficacy. The high levels of vaccine efficacy and safety observed in clinical trials have been subsequently confirmed by their real-world effectiveness and the limited number of serious adverse events following widespread vaccinations in the United States and other countries. The safety of these products was a top priority in their development, and the clinical trials for these vaccines recruited a robust and diverse cohort of participants to help ensure that they are as safe as possible for all individuals. Vaccination and adherence to public health measures are the proven interventions that are particularly important as we work to address severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants that may emerge with increased transmissibility or pathogenicity.



The impressive safety and effectiveness data of these vaccines in clinical trials and under real-world conditions would not have been possible without the participation of, and contributions from, minority communities. I strongly recommend everyone who is eligible to receive the COVID-19 vaccine. In addition, I am committed to continuing to work with leaders in minority communities to understand the motivations behind vaccine hesitancy and develop strategies to communicate the safety and efficacy of the available COVID-19 vaccines in the most effective manner possible.

**Submitted by Rep. Tom Cole*****RUNX1-FPD Clinical Research Study***

Question: Germline mutations in the gene RUNX1 frequently lead to blood cancers, and I want to commend NCI for working with the National Human Genome Research Institute to support the RUNX1-FPD Clinical Research Study, which offers researchers the opportunity to monitor the genomic evolution of cancer in real time. While germline RUNX1 mutations are rare, I understand that NIH-funded research in this area could have useful implications for the fields of hematology and oncology. How can deepening our understanding of and ultimately developing cancer prevention strategies for inherited blood cancer predisposition syndromes like RUNX1 familial platelet disorder advance the entire cancer research field forward?

**NIH Response:**

The RUNX1 gene regulates the development of blood cells (hematopoiesis), controlling other genes that help determine the fate of hematopoietic stem cells, which have the potential to develop into all types of mature blood cells, including platelets. Platelets are cells that help blood to clot. Inherited mutations in the RUNX1 gene cause familial platelet disorder with associated myeloid malignancies (RUNX1-FPDMM) and predispose individuals to some types of blood cancers. Although genetic predisposition to solid tumors such as breast and colon cancers has been widely recognized over the past several decades, the contribution of inherited genetic disorders related to blood cancer is a more recent field of study.

There are many instances where understanding the molecular basis for a rare inherited disease has provided insight into more common forms of a particular disease. For example, BRCA1 and BRCA2 mutations were discovered as hereditary breast cancer genes but are also relevant to sporadic (non-hereditary) breast cancers, ovarian cancers, and some hereditary forms of colon cancer. Similarly, understanding the blood cancers associated with RUNX1-FPDMM may lead to improved understanding of other types of blood cancers as well.

Research efforts across the National Institutes of Health (NIH) are underway to better understand RUNX1-FPDMM. Investigators funded by the National Heart, Lung, and Blood Institute (NHLBI) are studying cells from people with this disorder to better understand key target genes regulated by RUNX1 and their role in hematopoiesis ([reporter.nih.gov/project-details/10083753](http://reporter.nih.gov/project-details/10083753)). This work could also yield a better understanding of genetic pathways that lead to blood cancers, as well as the blood clotting mechanisms that contribute to cardiovascular disease. Investigators at the National Human Genome Research Institute (NHGRI), along with intramural scientists at the National Cancer Institute (NCI), are conducting a natural history study at the NIH Clinical Center (CC) that is intended to identify and follow patients with RUNX1 mutations to hopefully identify biomarkers that can predict which patients will develop cancers ([www.genome.gov/Current-NHGRI-Clinical-Studies/hematologic-and-premalignant-conditions-associated-with-RUNX1-mutation](http://www.genome.gov/Current-NHGRI-Clinical-Studies/hematologic-and-premalignant-conditions-associated-with-RUNX1-mutation); [clinicalstudies.info.nih.gov/ProtocolDetails.aspx?id=2019-HG-0059](http://clinicalstudies.info.nih.gov/ProtocolDetails.aspx?id=2019-HG-0059); and [clinicaltrials.gov/ct2/show/NCT03854318](http://clinicaltrials.gov/ct2/show/NCT03854318)). To date, the study has enrolled 198 patients from 55

families, representing the largest FPDMM cohort being followed prospectively at a single institution in the world.

Studying RUNX1-FPDMM will have broader significance than just this rare disease. Germline (inherited) predisposition to hematopoietic malignancies is often under-diagnosed, with recent studies indicating that 10-30 percent of RUNX1 mutations detected in acute myeloid leukemias are inherited, which is much more common than previously appreciated ([pubmed.ncbi.nlm.nih.gov/32315381/](http://pubmed.ncbi.nlm.nih.gov/32315381/)). In addition, FPDMM can serve as a model to study the development of leukemia, since researchers can monitor individuals with the RUNX1 mutation before they develop leukemia to identify factors associated with cancer risk and to map tumor evolution.

**Submitted by Rep. Andy Harris**

***Gain of Function***

Could the NIH identify by definition, and as adjudicated by NIH in award funding, what constitutes gain of function research?

**NIH Response:**

The U.S. Government and U.S. Department of Health and Human Services (HHS) define research that is reasonably anticipated to create, transfer, or use a potential pandemic pathogen (PPP) resulting from the enhancement of a pathogen's transmissibility and/or virulence in humans as enhanced PPP research. In 2017, HHS issued its *Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens (HHS P3CO Framework)*. This *HHS P3CO Framework* is responsive to and in accordance with the *Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight* issued by the Office of Science and Technology Policy (OSTP). The *HHS P3CO Framework* is intended to guide HHS funding decisions on proposed enhanced PPP research and seeks to preserve the benefits of life sciences research involving enhanced PPPs while minimizing potential biosafety and biosecurity risks.

Could you provide a list of current NIH grantees in Russia and China, and of grantees known to your knowledge to use NIH funding to conduct research in Russia or China?

**NIH Response:**

The National Institutes of Health (NIH) does not currently support the conduct of research subject to the *HHS P3CO Framework* in Russia or China by any grantees.

***Wuhan Institute of Virology Funding / Gain of Function Experiments***

In funding "Understanding the Risk of Bat Coronavirus Emergence" (1R01AI110964-01) to the EcoHealth Alliance, Inc, with Principal Investigator Peter Daszak, the grant cites that it would:

"Test predictions of CoV inter-species transmission. Predictive models of host range (i.e. emergence potential) will be tested experimentally using reverse genetics, pseudovirus and receptor binding assays, and virus infection experiments across a range of cell cultures from different species and humanized mice."

A subsequent paper was published on November 30, 2017 in the PLOS Pathogens Journal, "Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus," which cited NIH funding for this same R01. The paper explained:

“In this study, we confirmed the use of human ACE2 as receptor of two novel SARSr-CoVs by using chimeric viruses with the WIV1 backbone replaced with the S gene of the newly identified SARSr-CoVs.”

...

Using the reverse genetics technique we previously developed for WIV1 [23], we constructed a group of infectious bacterial artificial chromosome (BAC) clones with the backbone of WIV1 and variants of S genes from 8 different bat SARSr-CoVs.”

...

“we also constructed infectious clones with the S gene of Rs4081, Rf4075, Rs4085, Rs4235 and As6526, which all contained the deletions in their RBD. These 7 strains, plus Rs4874 and the previously studied WIV1 and RsSHC014, could represent all types of S variants of SARSr-CoVs in the location (S3A Fig). However, none of the strains with deletions in the RBD could be rescued from the Vero E6 cells.”

Was the NIH aware of these experiments? At the hearing, you testified that the NIH did not sponsor any gain of function research with this grant. Therefore, the NIH does not consider the research conducted as part of the above referenced actions to constitute gain of function, correct?

**NIH Response:**

None of the research approved by the National Institutes of Health (NIH) in the grant award to EcoHealth Alliance, ‘Understanding the Risk of Bat Coronavirus Emergence’ (1R01AI110964-01) met the criteria to be classified as research involving enhanced potential pandemic pathogens (ePPP), and therefore falls outside the scope of oversight of the U.S. Department of Health and Human Services (HHS) Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens (HHS P3CO Framework). The term “gain of function” has a common usage in scientific research, but only certain types of “gain of function” research are captured by the HHS P3CO Framework.

Prior to the release of the HHS P3CO Framework, the National Institute of Allergy and Infectious Diseases (NIAID) reviewed the grant under the *U.S. Government Gain-of-Function Deliberative Process and Research Funding Pause on Selected Gain-of-Function Research Involving Influenza, MERS and SARS Viruses* (funding pause) and determined that the proposed research did not meet the criteria described in the funding pause. This determination was based upon the following:

- the chimeric viruses created would contain only small portions of evolutionarily distant bat coronaviruses and
- research published in peer-reviewed scientific journals demonstrated that similar chimeric viruses exhibited reduced pathogenicity.

For these reasons, it was not reasonably anticipated that the chimeric viruses developed under the grant would have enhanced pathogenicity and/or transmissibility in mammals via the respiratory route, and NIAID determined that the funding pause did not apply to this grant. NIAID included a requirement for the grantee that if any of the chimeric viruses generated under the grant showed evidence of enhanced virus growth greater than

ten times that of the original virus from which they were created, the grantee must immediately stop all experiments with the viruses and provide NIAID and the Wuhan Institute of Virology Institutional Biosafety Committee with the relevant data and information related to these unanticipated outcomes.

When the HHS P3CO Framework was released in December 2017, the funding pause was lifted. NIAID reviewed the grant under the HHS P3CO Framework and determined that the experiments to generate SARS-like or MERS-like chimeric coronaviruses were not subject to the HHS P3CO Framework, which covers *research that is reasonably anticipated to create, transfer, or use potential pandemic pathogens resulting from the enhancement of a pathogen's transmissibility and/or virulence in humans*. Therefore, NIH did not approve the kind of “gain of function” research warranting the additional and unique P3CO oversight identified by stakeholders during extensive prior policy development. At the time of this determination, NIAID revised the terms and conditions of the award to indicate that should experiments proposed in this award result in a virus with enhanced growth by more than ten times compared to strains found in nature, the grantee must notify NIAID immediately and that further research involving the resulting virus(es) may require review by HHS in accordance with the HHS P3CO Framework.

It is critical to emphasize that the body of science reported under the grant, including the bat coronavirus sequences published in the scientific literature, showed that the viruses studied were evolutionarily quite distant from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and could not have been the source of SARS-CoV-2.

### **ARPA-H**

You cited the Defense Advanced Research Projects Agency (DARPA) as the role model for an ARPA-H located within NIH. A recent article in the Journal of American Affairs, “Inside Operation Warp Speed: A New Model for Industrial Policy,” cited the critical role of DARPA in the advancement of mRNA vaccine technologies. DARPA’s work followed by the Biomedical Advanced Research and Development Authority (BARDA) were critical to the success of these technologies. Both DARPA and BARDA are intentionally independent from other portions of the biomedical research industry.

- 1) Have you evaluated the impact of including ARPA-H as part of NIH against the relevant history and independence of DARPA and BARDA?

#### **NIH Response:**

The Advanced Research Projects Agency for Health (ARPA-H) would be modeled after the Defense Advanced Research Projects Agency (DARPA) in order to establish a culture of championing innovative ideas, with a flat, nimble organizational structure, tenure-limited program managers with a high degree of autonomy, and a milestone-based approach. ARPA-H will be tasked with building high-risk, high-reward capabilities or platforms to drive biomedical breakthroughs – ranging from molecular to societal – that would provide transformative solutions for all patients.

Although DARPA is an excellent inspiration for ARPA-H, it is not a perfect model for biomedical and health research. It serves the needs of a single customer, the U.S. Department of Defense (DOD), and its mission is focused on national security. Its projects typically involve engineered systems. By contrast, health breakthroughs (i) interact with biological systems that are much more complex and more poorly understood than engineered systems, requiring close coupling to a vast body of biomedical knowledge and experience; (ii) interact with a complex world of many customers and users—including patients, hospitals, physicians, biopharma companies, and payers; (iii) interact in complex ways with human behavior and social factors; and (iv) require navigating a complex regulatory landscape. ARPA-H can learn from DARPA but will need to pioneer new approaches.

ARPA-H will fund biomedical research with a focus on use-driven capabilities to transform medicine, similar to the National Institutes of Health's (NIH) goal of turning discovery into health to improve the lives of all Americans. In order to avoid duplication, ARPA-H will coordinate with existing programs and NIH's Institutes, Centers, and Offices (ICOs). While ARPA-H will be housed in NIH, it will be autonomous and distinct from NIH's ICOs. ARPA-H would also be distinct from other existing agencies, such as the Biomedical Advanced Research and Development Authority (BARDA), which focuses on medical countermeasures for public health security threats.

- 2) Do you have the public-private partnership capabilities and capacities equivalent to BARDA or DARPA?

**NIH Response:**

The Administration is requesting authorities that would provide ARPA-H with similar capabilities for public-private partnerships as those of BARDA and DARPA.

- 3) Do you have the antitrust capabilities and capacities equivalent to BARDA?

**NIH Response:**

The Administration is requesting authorities that would provide ARPA-H with similar antitrust capabilities and capacities as BARDA.

- 4) Could you provide the analysis for the decision to house ARPA-H at NIH? And given the historic funding level, will this entity be designated as a Center or an Institute?

**NIH Response:**

ARPA-H will have a distinct culture as an independent agency within the NIH, with the expectation that ARPA-H can leverage NIH's infrastructure and expertise, and collaborate closely with NIH's Institutes, Centers, and Offices (ICOs) within the NIH enterprise. ARPA-H will not be organized in the same manner as a traditional ICO since it will have a unique mission, require different approaches to grant award review criteria, and focus more on large-scale, high-risk high-reward projects.

- 5) Was ARPA-H ever considered as an FFRDC?

**NIH Response:**

Unlike Federally Funded Research and Development Centers (FFRDC), ARPA-H will have federal authority to set out a bold vision of innovation and the ability to collaborate with other key agencies such as the U.S. Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), BARDA, and the Centers for Medicare and Medicaid Services (CMS)—to identify critical needs and opportunities and to partner on complex projects that interact, for example, with public health infrastructure or medical regulation.

ARPA-H would utilize public-private partnerships to achieve transformational change with the distinct goal of creating a dynamic culture of creativity that can be nimble and willing to fail in order to achieve solutions that have eluded researchers within the current biomedical ecosystem. With a sense of urgency, ARPA-H would focus on time-limited projects with goals, benchmarks, and accountability with the expectation that if specific milestones are not met, projects may be terminated.

- 6) Could you provide additional detail to the functions of with respect to ARPA-H and NCATS? And, how will you avoid redundancy?

**NIH Response:**

ARPA-H will have a culture distinct from all NIH's ICOs, including National Center for Advancing Translational Sciences (NCATS), that follow traditional peer review systems for awarding grants and contracts, but will coordinate with NIH in ways that strengthen and help catalyze transformative discoveries.

ARPA-H's proposed mission – to benefit the health of all Americans by catalyzing health breakthroughs that cannot readily be accomplished through traditional research or commercial activity – differs from NCATS's creative mission to apply scientific reasoning to improve the process by which we translate discoveries into health interventions. The ultimate goals are similar, but ARPA-H will focus on platforms for discovery whereas NCATS focuses on better translating those discoveries. For example, approximately 90 percent of NCATS's resources support a national network of clinical research centers and a drug screening hub. While NCATS's modestly sized Cures Acceleration Network is aligned with the general direction of ARPA-H, they will be synergistic and complementary rather than duplicative. Close collaboration on ideas and strategies will serve to avoid redundancy and, since ARPA-H will not have its own high-tech laboratory, ARPA-H will utilize and leverage NCATS' intramural capabilities.

***COVID-19 Therapeutic Funding***

How has NIH worked with BARDA to ensure that COVID-19-designated therapeutic (or therapeutic, vaccine, and diagnostic) research dollars are best utilized to advance promising candidates? Was this funding awarded through NIH, and if so, how much? Could you specify by Rescue Act and whether said funds were sent to the DAIDS within NIAID?

**NIH Response:**



The National Institutes of Health (NIH) and the Biomedical Advanced Research and Development Authority (BARDA) work alongside other Federal agencies and private companies to accelerate the development and deployment of medical countermeasures (MCMs), including MCMs against coronavirus disease 2019 (COVID-19). NIH and BARDA advanced the overall strategy to address COVID-19—including through establishment of USG partnerships, market research efforts, and early funding solicitations—and identified characteristics of vaccines, therapeutics, and diagnostics that could be targeted for rapid development. This close collaboration between NIH and BARDA continues to ensure that research dollars are appropriately allocated to advance promising MCMs.

NIH and BARDA continuously communicate to coordinate USG investments in MCMs to combat COVID-19. For example, NIH regularly attends the BARDA-led CoronaWatch meetings, which provide companies with technical feedback and directs them to agencies with the resources most relevant for their specific stage of product development. This coordination allows the rapid identification of opportunities and gaps in USG support for priority technologies and how to address them.

NIH and BARDA also co-led the 2019-novel Coronavirus Medical Countermeasures Task Force (MCM TF), which also included representatives from the U.S. Department of Health & Human Services' (HHS) Centers for Disease Control and Prevention (CDC), and U.S. Food and Drug Administration (FDA) and the U.S. Department of Defense (DOD), U.S. Department of Homeland Security (DHS), U.S. Department of Veterans Affairs (VA), and U.S. Department of Agriculture (USDA). The MCM TF consisted of four working groups—Clinical, Diagnostics, Therapeutics, and Vaccines—and each was co-led by BARDA and NIH chairs. The MCM TF's prioritization of vaccine and therapeutic candidates as well as classes of therapeutics and types of diagnostics tests served as the strategic foundation for research investments of Operation Warp Speed (OWS),

In April 2020, NIH launched the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public-private partnership to advance a coordinated USG research agenda for prioritizing and speeding development of the most promising treatments and vaccines. ACTIV brought together resources from NIH, BARDA, FDA, VA, CDC, DOD, and major pharmaceutical companies to expedite COVID-19 clinical trials. NIH has taken steps to ensure the ACTIV partnership is closely interconnected and complementary with other COVID-19 efforts, including those led by the BARDA co-led MCM TF and later through OWS, now known as the Countermeasures Acceleration Group (CAG).

The National Institute of Allergy and Infectious Diseases (NIAID) established the COVID-19 Prevention Network (CoVPN) by leveraging four existing NIAID-funded clinical trials networks in cooperation with the DOD. The CoVPN enrolled tens of thousands of volunteers in large-scale clinical trials to test a variety of investigational vaccines and monoclonal antibodies intended to protect people from COVID-19. The

CoVPN also participated in harmonized protocols developed in collaboration with BARDA, the ACTIV public-private partnership, and vaccine manufacturers. In addition, the CoVPN and NIH participated in BARDA's project coordination teams, which provide program management and technical support to each of the programs funded under the CAG.

NIH also is partnering with BARDA, CDC, FDA, and the Defense Advanced Research Projects Agency (DARPA) on the Rapid Acceleration of Diagnostics (RADx<sup>SM</sup>) initiative to speed innovation in the development, commercialization, authorization, and implementation of technologies to test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19 disease.

Through these collaborative efforts, NIH and BARDA continue to work together to ensure that we are leveraging the intrinsic strengths from public and private sector partners to achieve an unprecedented level of scientific achievement during the COVID-19 pandemic. This close coordination ensures that the funding provided to NIH and BARDA is used in the most effective way possible.

On behalf of HHS under delegated authority, NIH has administered funding for COVID-19 therapeutics research under the Coronavirus Aid, Relief, and Economic Security (CARES) Act, the Coronavirus Response and Relief Supplemental Appropriations Act (CRRSA), and the American Rescue Plan (ARP) Act. As of September 30, 2021, the total obligated amounts from these supplemental appropriations are \$861.4 million, \$625.6 million, and \$198.9 million, respectively. Within these totals, NIAID's Division of AIDS (DAIDS) has managed \$169.0 million, \$373.1 million, and \$40.2 million respectively.

How would NIH rate its historic partnership with BARDA through the PHEMCE or otherwise?

**NIH Response:**

The National Institutes of Health (NIH) and the Biomedical Advanced Research and Development Authority (BARDA) have a close working relationship, which has facilitated the unprecedented speed of the development of safe and effective coronavirus disease 2019 (COVID-19) diagnostic tests, therapeutics, and vaccines. The United States Government (USG) response to the COVID-19 pandemic has strengthened existing coordination mechanisms and led to the development of the new partnerships described above. It should be noted that this coordination was made possible, in part, because of the long-standing Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) structure. The existing relationships developed through the PHEMCE and the understanding of the capabilities, portfolios, and expertise of the constituent partners facilitated by previous work under PHEMCE allowed for the Medical Counter Measures Task Force and Operation Warp Speed (now Countermeasures Acceleration Group) to be quickly established, staffed, and executed.

NIH and BARDA will continue to build on these efforts to coordinate the identification and development of additional safe and effective diagnostic tests, therapeutics, and vaccines for COVID-19, other infectious diseases, as well as chemical, biological, radiological, and nuclear threats.

What therapeutics have been developed from the NIH ACTIV trial that BARDA was not previously already developing?

**NIH Response:**

Below is a list of therapeutic compounds tested in the NIH Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) trials. AZD7442, SAB-185, Lenzilumab, and LY-CoV-555 are listed in the Biomedical Advanced Research and Development Authority's (BARDA's) COVID-19 medical countermeasures portfolio and were previously under development by BARDA.

([www.medicalcountermeasures.gov/app/barda/coronavirus/COVID19.aspx?filter=therapeutic](http://www.medicalcountermeasures.gov/app/barda/coronavirus/COVID19.aspx?filter=therapeutic)).

| Company              | Therapeutic                                                   | Class                        | Administration         |
|----------------------|---------------------------------------------------------------|------------------------------|------------------------|
| <b>ACTIV-1</b>       |                                                               |                              |                        |
| AbbVie               | Cenicriviroc                                                  | Immune Modulator             | Oral                   |
| BMS                  | Orencia® (abatacept)                                          | Immune Modulator             | Intravenous            |
| Janssen              | Remicade® (Infliximab)                                        | Immune Modulator             | Intravenous            |
| <b>ACTIV-2</b>       |                                                               |                              |                        |
| AstraZeneca          | AZD7442                                                       | Monoclonal Antibody Cocktail | Intramuscular          |
| AstraZeneca          | AZD7442                                                       | Monoclonal Antibody Cocktail | Intravenous            |
| Brii Biosciences     | Brii-196 & Brii-198                                           | Monoclonal Antibody Cocktail | Intravenous            |
| Bristol Myers Squibb | BMS-986414 and BMS-986413 (also known as C135-LS and C144-LS) | Monoclonal Antibody Cocktail | Subcutaneous Injection |
| Eli Lilly            | LY-CoV-555                                                    | Monoclonal Antibody Single   | Intravenous            |

|                                |                                                              |                                 |             |
|--------------------------------|--------------------------------------------------------------|---------------------------------|-------------|
| SAB<br>Biotherapeutics         | SAB-185                                                      | Polyclonal antibody             | Intravenous |
| Sagent                         | Camostat Mesylate                                            | Antiviral                       | Oral        |
| Synairgen                      | SNG001 IFN-beta                                              | Immune Modulator                | Inhaled     |
| <b>ACTIV-3</b>                 |                                                              |                                 |             |
| AstraZeneca                    | AZD7442                                                      | Monoclonal<br>Antibody Cocktail | Intravenous |
| Brii Biosciences               | Brii-196 & Brii-198                                          | Monoclonal<br>Antibody Cocktail | Intravenous |
| Eli Lilly                      | LY-CoV-555                                                   | Monoclonal<br>Antibody Single   | Intravenous |
| Giliad/NeuroRx                 | Zyesami® (aviptadil<br>acetate) and Veklury®<br>(remdesivir) | Immune<br>Modulator/Antiviral   | Intravenous |
| GSK-Vir                        | VIR-7831                                                     | Monoclonal<br>Antibody Single   | Intravenous |
| Molecular<br>Partners/Novartis | Ensovibep (MP0420)                                           | DARPin                          | Intravenous |
| Pfizer                         | PF-07304814                                                  | Protease inhibitor              |             |
| <b>ACTIV-4</b>                 |                                                              |                                 |             |
| BMS/Pfizer                     | Elitiquis ® (apixaban)                                       | Anticoagulant                   | Oral        |
| BMS/Pfizer                     | Aspirin                                                      | Antiplatelet                    | Oral        |
| Other                          | Un-fractionated (UF)<br>Heparin                              | Anticoagulant                   | Intravenous |
| Other                          | Unfractionated<br>Heparin and P2Y12<br>Inhibitors            | Anticoagulant                   | Intravenous |
| Other                          | Low Molecular Weight<br>(LMW) Heparin                        | Anticoagulant                   | Injection   |
| Constant<br>Therapeutics       | TXA127                                                       | Mas Receptor<br>Agonist         | IV          |

|                             |                                           |                            |             |
|-----------------------------|-------------------------------------------|----------------------------|-------------|
| Trevena                     | TRV027                                    | AT1R Beta-arrestin Agonist | IV          |
| Other                       | Therapeutic Heparin and P2Y12 Inhibitors  | Anticoagulant              |             |
| Other                       | Prophylactic Heparin and P2Y12 Inhibitors | Anticoagulant              |             |
| APN01                       |                                           |                            |             |
| Fostamatinib                |                                           |                            |             |
| ACTIV-5                     |                                           |                            |             |
| AbbVie/Boehringer Ingelheim | Skyrisi- (risankizumab)                   | Immune Modulator           | Intravenous |
| Humanigen                   | Lenzilumab                                | Immune Modulator           | Intravenous |
| Alexion                     | Danicopan                                 | Factor D Inhibitor         | Oral        |
| ACTIV-6                     |                                           |                            |             |
| Ingenus                     | Ivermectin                                | Immune Modulator/Antiviral | Oral        |
| Apotex                      | Fluvoxamine                               | Immune Modulator/Antiviral | Oral        |
| GlaxoSmithKline             | Fluticasone                               | Immune Modulator           | Oral        |

#### ***NIH fetal tissue and related research***

Please provide how the NIH obtained these specimens of mid-second trimester aborted fetuses. Specifically, how did the grantee obtain the specimens, did it involve fetal decapitation, and what was the approval review process and adjudication for this decision?

#### **NIH Response:**

The National Institutes of Health (NIH) understands that the question refers to research described in a published article, *Development of humanized mouse and rat models with full-thickness human skin and autologous immune cells*. That publication cites support by the NIH-National Institute of Allergy and Infectious Diseases (NIAID) (R21AI135412) and the NIH-Fogarty International Center (D43TW010039). The NIH Award P30CA047904 supported (in part) the University of Pittsburgh Biospecimen Core. NIH did not obtain fetal tissue specimens—the extramural researchers (all but one of the authors were at the University of Pittsburgh) would have done so. This paper includes additional information regarding the research methods.

Regarding review at the University of Pittsburgh: the paper states that "Written informed consent of the maternal donors was obtained in all cases, under a protocol reviewed and approved by the Institutional Review Board (IRB) of the University of Pittsburgh; approved guidelines and federal/state regulations were adhered to for all procedures. The use of de-identified human fetal tissues to construct humanized rodents was reviewed and approved by the University of Pittsburgh IRB Office. The use of de-identified human fetal tissues did not constitute human subjects research as defined under federal regulations [45 CFR 46.102(d or f) and 21 CFR 56.102(c), (e), and (I)]. The use of human fetal liver-derived hematopoietic stem cells was reviewed and approved by the Human Stem Cell Research Oversight (hSCRO) at the University of Pittsburgh. The use of a biological agent (CA-MRSA), recombinant DNA, and transgenic animals were reviewed and approved by the Institutional Biosafety Committee (IBC) at the University of Pittsburgh. All animal studies/experimental protocols were reviewed and approved by the Institutional Animal Care and Use Committee (IACUC) at the University of Pittsburgh and were conducted following approved guidelines, which adheres to the NIH guidelines for housing and care of laboratory animals."

The applications to NIH for the awards cited in this paper underwent peer review for scientific merit and second-level review by the NIH Institute advisory councils. NIH requires that NIH-supported organizations, including the University of Pittsburgh, certify that they will comply with the NIH Grants Policy Statement, which summarizes NIH policies regarding the use of human fetal tissue in research and incorporates Federal statutory requirements for research with human fetal tissue (sections 498A and 498B of the PHS Act, 42 U.S.C. 298g-1 and 298g-2).

Federal law (42 USC 289g-2) prohibits any person from knowingly acquiring any human fetal tissue for *valuable consideration*. During your tenure at NIH, has the agency conducted any audits to confirm whether NIH grantees are in compliance with the statutory requirements regarding fetal tissue research?

**NIH Response:**

The National Institutes of Health (NIH) employs a long-standing and well-established system for working with funding recipients to ensure compliance with a host of laws, regulations, and policies, as summarized in the NIH Grants Policy Statement. When submitting a funding application for research involving fetal tissue, the designated representative of the external organization receiving the funding certifies that researchers using these samples are in compliance with applicable legal requirements. In addition, by accepting an award, funding recipients agree that they will follow all applicable legal requirements and the NIH's Grants Policy Statement, and they must be able to demonstrate their compliance. NIH also requires funding recipients to re-certify when additional funding is awarded that they are in compliance, and they are responsible for establishing internal procedural controls to ensure compliance.

Complete information about what happens when NIH becomes aware/suspects a grantee, contractor, or NIH employee is breaking the law can be found here: [oma1.od.nih.gov/manualchapters/management/1754/](http://oma1.od.nih.gov/manualchapters/management/1754/).

NIH is aware of other investigative activities. In 2016, the Select Investigative Panel on Infant Lives of the Committee on Energy and Commerce referred a number of entities for further investigation by the Department of Justice into possible violations of the law. Also in 2016, Senator Grassley, then chairman of the Committee on the Judiciary, referred a number of entities to the Department of Justice for investigation and potential prosecution ([www.grassley.senate.gov/news/news-releases/grassley-refers-planned-parenthood-fetal-tissue-procurement-organizations-fbi](http://www.grassley.senate.gov/news/news-releases/grassley-refers-planned-parenthood-fetal-tissue-procurement-organizations-fbi)). The U.S. Department of Health and Human Services (HHS), Office of the Inspector General also conducted a review of NIH processes in 2016.

NIH expects researchers to obtain informed consent from the donor for any NIH-funded research. The previous Administration required researchers seeking to use human fetal tissue to describe the process for obtaining written, voluntary, informed consent. This includes certifying that no enticements, benefits, or financial incentives were used at any level of the process to incentivize abortion or the donation of HFT. Is NIH continuing to require detailed descriptions from researchers of the informed consent obtained?

**NIH Response:**

Yes, as described in the April 16, 2021 notice [NOT-OD-21-111](https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-111.html) ([grants.nih.gov/grants/guide/notice-files/NOT-OD-21-111.html](https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-111.html)), the National Institutes of Health (NIH) continues to require a description of the planned written, voluntary, informed consent process (and other information) for competing applications as specified in [NOT-OD-19-128](https://grants.nih.gov/grants/guide/notice-files/NOT-OD-19-128.html) ([grants.nih.gov/grants/guide/notice-files/NOT-OD-19-128.html](https://grants.nih.gov/grants/guide/notice-files/NOT-OD-19-128.html)) and clarified in [NOT-OD-19-137](https://grants.nih.gov/grants/guide/notice-files/NOT-OD-19-137.html) ([grants.nih.gov/grants/guide/notice-files/NOT-OD-19-137.html](https://grants.nih.gov/grants/guide/notice-files/NOT-OD-19-137.html)). Investigators in the NIH Intramural Research Program must also affirm that informed consent was obtained per [NOT-OD-16-033](https://grants.nih.gov/grants/guide/notice-files/not-od-16-033.html) ([grants.nih.gov/grants/guide/notice-files/not-od-16-033.html](https://grants.nih.gov/grants/guide/notice-files/not-od-16-033.html)).

**Submitted by Rep. Chuck Fleischmann**

Concerned about other countries' ability to obtain vaccines quickly for their populations, the Administration recently announced that it will support a waiver of the World Trade Organization TRIPS Agreement, which would waive intellectual property protections for COVID-19 vaccines. I'm concerned because there are no guarantees that the companies or countries who seek to use vaccine manufacturer's intellectual property to make copies will be able to deliver safe and effective vaccines, or that their manufacturing processes will meet the strict regulatory standards necessary for authorization. There are already reports of counterfeit vaccines being used to exploit vulnerable populations in the U.S. and around the world.

- Are you concerned that giving away intellectual property via a TRIPS waiver could make worse the existing problem of counterfeit and low-quality vaccines in the market, possibly both endangering lives and undermining public confidence in the vaccines that have been proven safe and effective?

**NIH Response:**

The terms of any TRIPS waiver for COVID-19 vaccines are under negotiation and will include protections to ensure the safety and efficacy of COVID-19 vaccines. Other Departments and Agencies may have additional information.

The Administration recently endorsed the idea of waiving intellectual property (IP) protections for COVID-19 vaccines, in the hopes that it will speed up manufacturing of the vaccines around world. However, we know that vaccine developers are already experiencing constraints in everything from raw materials to fill-finish capacity critical to producing and administering vaccines. These are complex products – I have read that one of the authorized vaccines requires 280 different components produced by suppliers in 19 different countries. If the companies who developed the vaccines are forced to surrender their IP, they will have to compete with other companies for what are already scarce resources with companies who are unlikely to have the experience and expertise to quickly manufacture the necessary vaccines.

- Are you concerned that diverting critical supplies from manufacturers with proven track records for delivering high-quality, safe and effective vaccines could actually worsen the supply chain constraints we're currently seeing, and not just for COVID vaccines, but also non-COVID-19 medicines such as oncology and other infectious diseases?

**NIH Response:**

The terms of any TRIPS waiver for COVID-19 vaccines are under negotiation. Through this and other efforts, the Administration is working to improve supply chains to meet world-wide demands for safe and effective COVID-19 vaccines. Other Departments and Agencies may have additional information.



The U.S. biomedical R&D ecosystem – which of course includes the National Institutes of Health along with innovative biopharmaceutical companies and world class universities – is the envy of the world. It is well documented that one of the foundations of that ecosystem and a key factor in its success is the incentive that patents create for companies to invest billions of dollars over long time horizons with no guarantee of any financial returns. And yet, in the face of a global pandemic, we are contemplating forcing companies to surrender their patents. It seems unwise to me to send innovators the message that the larger the health crisis, the less we will respect your IP.

- As a leader of an essential part of this ecosystem, how do you believe that the waiving of patent rights for these companies would affect their ability to partner with the government to address future pandemics?

**NIH Response:**

The National Institutes of Health (NIH) is not able to speak for these companies, but the Administration wants to ensure that U.S. Government and private sector companies continue to have strong collaborations to address future pandemics.

Waiving intellectual property is not the same thing as a plan for the U.S.’s global vaccination strategy. In fact, waiving the IP for the COVID vaccines without a comprehensive strategy only jeopardizes our ability to respond to future pandemics without an actual benefit for citizens. Other types of initiatives, such as PEPFAR, have been successful in the past.

- Do you think a similar public-private partnership, leveraging the existing manufacturers that are already working hard in this space, would be a better approach?

**NIH Response:**

Multiple approaches aim to address vaccine shortages. Public-private partnerships are one promising approach. The National Institutes of Health (NIH), other agencies, the private sector, and international organizations such as the World Health Organization (WHO) are developing such efforts to address the challenge.

Remarks on ARPA-H in Dr. Collins’ written testimony expressly mention “leveraging novel public-private partnerships”.

- What will ARPA-H’s mandate or plans be in the realm of global health security, such as developing vaccines and other countermeasures against COVID-19 or potential future pandemic threats? And if there are plans, would this involvement by ARPA-H fill a need globally that is unfilled?

**NIH Response:**

ARPA-H is envisioned to revolutionize methods to prevent, treat, and even cure diseases that the current biomedical research ecosystem has not achieved to date. As such, ARPA-H will work with colleagues in DARPA and BARDA to fill unmet needs in the health of Americans, global health, and global health security.

- Would that include global partnerships and those seeking to develop innovations for global access and application, or primarily for domestic use?

**NIH Response:**

Global partnerships will be encouraged in pursuit of developing innovations with global and domestic application.

In the American Rescue Plan legislation, USAID was provided around \$5 billion for global COVID-19 response, including \$905 million for Global Health Programs (in addition to and \$3 billion for humanitarian response and nearly \$1 billion for economic stabilization and relief). The legislation directed the Administration to contribute to “a multilateral vaccine development partnership to support epidemic preparedness,” which is understood to be the Coalition for Epidemic Preparedness Innovations, or CEPI – itself a “novel public-private partnership.”

- What is the status of the contribution to CEPI from the funds made available in the American Rescue Plan legislation more than two months ago?

**NIH Response:**

As this question relates to non-HHS funding, HHS defers to USAID for response.

- Does a delay in providing that contribution mean that the Administration is waiting to see what remains after other priorities are met to determine the level of funding?

**NIH Response:**

As this question relates to non-HHS funding, HHS defers to USAID for response.

- Would you see ARPA-H as possibly partnering and contributing financially to CEPI as a novel public-private partnership, or would that be somehow redundant of what the plans are for ARPA-H?

**NIH Response:**

At this stage of planning, no public-private partnerships are being ruled out, as it would be up to the ARPA-H Director and the program directors who would be given autonomy to support high-risk, high-reward projects within limited time frames.

**Submitted by Rep. Jaime Herrera Beutler*****Alzheimer's Research***

Question: Alzheimer's is one of the most expensive diseases in America. While recent funding increases have enabled significant advances in understanding the complexities of the disease, investment in Alzheimer's research is only a fraction of what's been applied over time, with great success, to address other major diseases. The NIH Professional Judgment Budget for Alzheimer's Disease and Related Dementias for Fiscal Year 2022 requests an additional \$289 million for Alzheimer's research.

- What type of cutting-edge science could this additional investment fund? How can we target funding to better understand the risks and protective factors in individuals across diverse populations?

**NIH Response:****What type of cutting-edge science could this additional investment fund?**

Targeted investment in Alzheimer's Disease and Alzheimer's Disease Related Dementias (AD/ADRD) research would further advance knowledge and understanding about preventing dementia and improving diagnostics, treatments, and care of those living with these diseases. Continued prioritization would also drive efforts to develop novel biomarkers for use as screening tests and to monitor treatment response, identify and test new drug candidates, advance comprehensive models of care, explore disease risk and protective factors, and improve the understanding of the role of genetics and other disease mechanisms. As a specific example, researchers supported by the National Institutes of Health (NIH) continue to work to develop blood tests to detect proteins that form clumps in the brain, including amyloid and two forms of tau (ptau181 and ptau217) to help diagnose Alzheimer's. Recent work indicates that neurofilament light chain (NfL), a component of a neuron's "skeleton," may be a promising blood biomarker that indicates neurodegeneration and could be useful for the detection of several neurodegenerative diseases.

NIH could increase support for late-stage clinical trials testing novel drug candidates and importantly, the testing of repurposed drugs that are not typically developed for AD/ADRD by pharmaceutical companies. Moreover, NIH could also expand the critical early stages of the drug discovery pipeline by providing funding for initiatives aimed at evaluating, prioritizing, and advancing the next generation of AD drug targets into full-fledged drug discovery programs. As one specific example, the National Institute on Aging (NIA) has a very successful pre-clinical drug development program that has resulted in 12 new, first-in-class drugs (i.e., cutting-edge drugs) that are currently undergoing testing in clinical trials.

Additional areas of promise include research on impact of sex difference on the biology of the disease and on the relationship of genes and environment to AD risk and resilience, across diverse populations.

Previous Alzheimer's funding helped support construction of a new intramural research facility devoted to AD/ADRD research in Bethesda, Maryland. The Center for Alzheimer's

Disease and Related Dementias (CARD) supports basic, translational, and clinical research. Although the CARD facility is expected to open in 2022, studies are already in progress. In early 2021, CARD investigators and their collaborators began efforts to create “personalized” stem cells for studying dementia. This project, one of the first to be supported through CARD, is designed to engineer cell models of disease-causing gene mutations from multiple brain disorders, including Alzheimer’s, frontotemporal dementia, and amyotrophic lateral sclerosis, dementia with Lewy bodies, and Parkinson’s disease dementia. This project will produce a library of cell lines that will be freely available and can be used for disease modeling and drug development.

**How can we target funding to better understand the risks and protective factors in individuals across diverse populations?**

NIH is funding several efforts to understand the risk and protective factors for AD/ADRD across diverse populations, and a recent NIH-supported National Academy of Sciences, Engineering, and Medicine AD/ADRD Decadal study<sup>31</sup> explores these important topics. NIH-supported population studies are underway to explore the health of populations over a long period of time, which helps researchers determine why some people develop these diseases while others do not. For this research, scientists aim to involve a large group of people who represent the diversity of the U.S. population and collect data from them covering a wide array of factors that might exacerbate or mitigate risk factors of disease.

With respect to better understanding the risks and protective factors in individuals across diverse populations, NIA has recently provided funding to increase the numbers of Black/African American and Hispanic/Latino participants in two of the primary nationally representative data sources for tracking the incidence and prevalence of dementia as well as longitudinal trends in dementia risk factors in the U.S. population. These additions to the Health and Retirement Study (HRS) are aiming also to collect longitudinal blood-based biomarkers of AD/ADRD if we can establish the feasibility of doing so and we can add novel biomarkers as they are validated both in the ongoing HRS as well as bio-banked samples from previous rounds of data collection. A recent initiative will add enhanced measures of educational experiences and cognitive function to existing studies to clarify the relationship between education, cognition, and risk of AD/ADRD, including the role of education in social disparities in AD/ADRD outcomes. Additional ongoing work seeks to harmonize data across nationally representative international longitudinal aging studies to support cross-national comparisons of the influence of institutional and cultural features on AD/ADRD risk factors and outcomes.

In addition, large-scale analyses of data collected from population studies have revealed many possible genetic risk factors for AD/ADRD. NIH’s Genetics of Alzheimer’s Disease Portfolio supports research to discover long-term treatments by identifying risk factor and protective genes and their underlying molecular pathways. Within this portfolio, the

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<sup>31</sup> <https://www.nationalacademies.org/our-work/decadal-survey-of-behavioral-and-social-science-research-on-alzheimers-disease-and-alzheimers-disease-related-dementias>

Alzheimer's Disease Sequencing Project (ADSP) supports studies to discover genes involved in Alzheimer's. This project involves more than 150 international investigators at 33 institutions. Data come from more than 60 cohorts of research participants. The aim of the sequencing project is to identify — in diverse populations — genes that increase risk for Alzheimer's and those that confer protection, as well as to provide insight into why some people with known risk factor genes do not develop the disease. To support ADSP, NIA released a solicitation in May 2021 to encourage research applications that would help to identify and confirm rare variants contributing to AD/ADRD in diverse cohorts, to enhance the probability of identifying potential therapeutic approaches for risk and prevention.

NIA is also funding the Study of Latinos—Investigation of Neurocognitive Aging (SOL-INCA) project. Initiated in 2015, the study is analyzing a wealth of data to examine how genetics and cardiovascular disease risk factors impact the prevalence of neurocognitive disorders among middle-aged and older participants. SOL-INCA scientists hope to find sociocultural risk and protective factors that may contribute to observed differences in dementia rates in the Latinx community. Its long-term goal is to identify targets that can be tested for actionable, culturally appropriate strategies for preventing or delaying the progression of dementia.

Through NIA-supported research, scientists also identified several novel DNA regions, or loci, unique to Blacks/African Americans living with Alzheimer's. Researchers found that the main biological pathways linked to Alzheimer's risk in African Americans largely overlapped with those in non-Hispanic white individuals, but there were several disease-associated genetic loci in these pathways that differed. This suggests that these overall pathways, including those responsible for immune response, intracellular transport, nervous system development, and fat metabolism, are not ethnic-specific and are important in understanding Alzheimer's disease risk across ethnic groups. The differences in the genetic regions in these pathways could prove to be additional targets for further investigation into racial/ethnic differences in risk. The researchers also found a link between kidney system development and Alzheimer's risk in African Americans, suggesting another novel disease mechanism to explore to better understand unique differences in disease risk between ethnic groups. African Americans are three times more likely to experience kidney failure than non-Hispanic whites. They are also more likely to have both dementia and kidney disease. Additional research to understand this connection will be important for the prevention and treatment of Alzheimer's disease in African Americans.

Question: Alzheimer's is a devastating condition for individuals and their family. By 2025, in my state of Washington, Alzheimer's disease is expected to increase by 16.7% in adults 65 and older. I've introduced a bipartisan bill, *the ENACT Act*, to increase the participation of underrepresented populations in Alzheimer's and other dementia clinical trials.

- How is NIH working to ensure that clinical trials enroll populations that are representative of the broader U.S. population, especially those most likely to need access to future treatments?

**NIH Response:**

To ensure that prevention and treatment interventions will be effective for all people living with Alzheimer's Disease and Alzheimer's Disease Related Dementias (AD/ADRD), investigators must recruit research participants from more diverse populations, including Blacks/African Americans and Hispanics/Latinos, who are at higher risk of dementia than white Americans. As a federal agency, the National Institutes of Health (NIH) is helping to coordinate, collaborate, and fund a range of activities to achieve this goal. The National Institute on Aging (NIA) has engaged in several activities to facilitate and enhance clinical study enrollment and retention. In 2018, NIA in collaboration with the Alzheimer's Association and many other stakeholders, developed and released the National Strategy for Recruitment and Participation in Alzheimer's and Related Dementias Clinical Research. The main goal of the national strategy is to engage broad segments of the public in the Alzheimer's and related dementias research enterprise, with a particular focus on underrepresented communities, so that studies with an aim to better understand and eventually cure these disorders can successfully and more quickly enroll and retain individuals. To complement and support the National Strategy, NIA established the Alzheimer's and Dementia Outreach, Recruitment, and Engagement (ADORE) platform in 2019. The platform is an online, searchable database of materials that facilitates resource sharing on topics related to the engagement, recruitment, and retention of participants in AD/ADRD studies.

NIA also has conducted annual focus groups, surveys, and stakeholder interviews to tailor recruitment materials for clinical studies to reach underrepresented populations more effectively. Using the findings from these research efforts, NIA has developed sets of materials and messaging, including videos and other multimedia, print ads, posters, and social media, tailored to specific underserved and vulnerable populations, including Asian Americans and Pacific Islanders (AAPI; 2021) available in English, Tagalog, Chinese, and Hindi; Spanish-speaking communities (2020) and available in both English and Spanish; and Black/African American audiences (2019). Additional communication activities to improve outreach to American Indians/Alaska Natives is underway in 2022.

In 2021, NIA launched OutreachPro, a web-based communication tool that enables health care professionals to more easily produce and brand tailored clinical trial recruitment materials and strategies. Designed to help reach multiple cultures and those who do not speak English, the tool enables the research community to access, adapt, and personalize materials that NIA has developed — and will continue to create — for underrepresented communities.

A key factor for improving enrollment is to help researchers monitor recruitment in near real time. To track, report, and manage enrollment data, NIA awarded a contract in 2020 to develop a unified Clinical Research Operations & Management System (CROMS). The tool

has been developed and NIA is currently working with grantees to enter their enrollment data into the system initially and then on a monthly basis. Through CROMS, NIA can track, manage, and report enrollment data and activities made possible via the NIA-funded clinical research portfolio. CROMS provides critical real-time information to ensure that NIA-supported clinical studies are making appropriate progress toward reaching their recruitment goals related to multiple underrepresented groups, including minorities. Using data from CROMS, NIA can then better implement, monitor, and rectify studies that perform poorly with respect to minority enrollment, as well as track studies that successfully enroll participants to identify and disseminate best practices to other grantees.

NIA continues to fund several projects with researchers to better understand the myriad of challenges scientists and potential participants face in clinical trials recruitment. In November 2018, NIA released a grant solicitation to encourage applications for projects that examine health disparities related to Alzheimer's, as well as strategies for recruitment and retention into clinical studies. To date, NIA has funded more than 115 projects in response to this initiative, and the funding opportunity will remain active for receipt of additional applications until November 2021. Collectively, projects will compare differences in risks for these conditions for men versus women, different racial and ethnic groups, rural communities, socioeconomically disadvantaged neighborhoods, and other societal and individual factors. Additionally, NIA funded Foundations of Representative Engagement, Valid, and Effective Recruitment (FOREVER) in Alzheimer's Research in September 2020. Through this project, researchers are developing and implementing novel methods for recruitment, engagement, and retention of groups underrepresented in research into AD/ADRD studies through community engagement and the NIA-funded Alzheimer's Disease Research Centers. The research team is also developing recruitment, engagement, and retention metrics and interventions, and establishing communications frameworks to improve literacy for both the general public and research communities. Conducting clinical trials with participants who are not only representative of the broader U.S. population but also most affected by the disease, as well as helping the field better recruit diverse participants is a high priority for NIA, and we will continue to strongly pursue these important issues.

### ***Stillbirth Research, ECHO***

Question: One of the areas of research that we continue to lack in is our understanding and data collection capacity on stillbirth. We know that more than 24,000 babies, most likely more, are stillborn each year, with the rate of early stillbirth remaining unchanged over time.

- How can we maximize NIH's resources to ensure we are funding research to ensure optimal birth outcomes for moms and babies, especially in areas like stillbirth?

#### **NIH Response:**

Stillbirth accounts for 60 percent of all deaths occurring around the time of birth, yet the causes of many of these are unknown. The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) supports research on the causes of stillbirth, its occurrence in populations, risk factors, and ways to prevent it from happening. For example, a recent NICHD-funded study looked at the role of umbilical cord abnormalities in stillbirth. It found that problems in the development of the umbilical cord can deprive the fetus of necessary oxygen and nutrients. Another NICHD-funded study developed a new ultrasound technique to monitor the placenta for impaired fetal blood flow early in pregnancy, which could help prevent stillbirth.

NICHD's Human Placenta Project aims to revolutionize our understanding of the placenta and ultimately improve the health of mothers and children. The goals of the project are to understand the role of the placenta in health and disease; develop new tools understand and monitor, in real time, placental development and function in normal and abnormal pregnancies; develop and evaluate non-invasive markers for prediction of adverse pregnancy outcomes; understand the contributions of placental development to long-term health and disease; and develop interventions to prevent abnormal placental development and hence improve pregnancy outcomes. This may one day help treat, and even prevent, a range of common pregnancy complications, including stillbirth, while providing insights into other areas of science and medicine.

- Are there opportunities to study and collect data on stillbirth by evaluating data from the ECHO study?

#### **NIH Response:**

The Environmental Influences on Child Health Outcomes (ECHO) program supports multiple, synergistic, longitudinal studies to investigate how environmental exposures—including physical, chemical, social, behavioral, biological, and natural and built environments—influence child health and development. The studies focus on five key pediatric outcomes that have a high public health impact 1) pre-, peri-, and postnatal outcomes, 2) upper and lower airway, 3) obesity, 4) neurodevelopment, and 5) positive health. The Program has two major components, the ECHO Cohorts – for observational research, and the ECHO IDeA States Pediatric Clinical Trials Network (ISPCTN)– for interventional research.



The ECHO Program includes 16 cohorts with ongoing recruitment during pregnancy and data from 37,000 completed pregnancies. Of those pregnancies, the Program has collected medical record abstraction data from about 30,000 women, which potentially includes information on stillbirths.

The ECHO Program is currently in the process of putting its data on a data platform with a target date for wider availability to the scientific community in Spring/Summer 2022.

### ***Maternal and Child Health***

Question: As you know, the United States is the only developed country to see maternal mortality rates rising and it is much worse for women of color. Maternal mental health is also far too pervasive with many cases unreported and untreated with perinatal mood and anxiety disorders (PMADs) affecting 1 in 7 pregnant and postpartum women that cost \$14.2 billion in 2017 alone.

- What is NIH doing to fund research to address maternal health issues, including the physical and psychological health of mothers throughout the first year of the birth of their children?

#### **NIH Response:**

Maternal health is a priority for the National Institutes of Health (NIH) and multiple NIH institutes have heavily invested in research to prevent maternal morbidity and mortality (MMM) and improve health for individuals, before, during, and after pregnancy. In FY 2020 NIH supported \$407 million of research on maternal health.

In a year that was dominated by both the coronavirus disease 2019 (COVID-19) pandemic and renewed calls to combat health disparities and inequities, NIH ensured these challenges were integrated into efforts to reduce MMM. In March 2020, researchers in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development's (NICHD) Maternal-Fetal Medicine Units Network designed the Gestational Research Assessments for CCOVID-19 (GRAVID) study, which evaluated data from more than 1,200 pregnant women at 33 hospitals across the country and found that pregnant COVID-19 patients with severe disease are at higher risk for cesarean delivery, postpartum hemorrhage, hypertensive disorders of pregnancy, and preterm birth. Data from the study is being shared with a larger registry to inform future studies of COVID-19's effects on pregnancy and maternal health.

NIH's IMPROVE (Implementing a Maternal health and PRenancy Outcomes Vision for Everyone) Initiative aims to build an evidence base that will improve maternal care and outcomes from pregnancy through one year postpartum. IMPROVE is co-led by NICHD, the NIH Office of the Director (OD), and the NIH Office of Research on Women's Health and engages over 30 NIH Institutes, Centers, and Offices to research the leading causes of maternal mortality in the United States—cardiovascular disease, infection, and immunity—as well as contributing health conditions or social factors, such as mental health disorders, diabetes, obesity, substance use disorders, and structural and healthcare system issues that disproportionately affect Black pregnant and postpartum women. IMPROVE prioritizes

comprehensive, interdisciplinary research that engages communities with high rates of maternal deaths and complications. This work will help create tailored, evidence-based solutions for pregnant and postpartum women.

- The opioid crisis is acute in our country and many babies are being exposed to drugs during pregnancy. What is NIH doing to address these youngest of victims and what are we learning?

#### **NIH Response:**

Each year, tens of thousands of babies are exposed to opioids during pregnancy, which can lead to poor fetal growth, preterm birth, withdrawal symptoms such as tremors, irritability, seizures, sleep, digestive, and feeding problems. The National Institutes of Health (NIH) is actively supporting research programs that can better prevent, understand, and address these problems. The trans-NIH Helping to End Addiction Long-term® (NIH HEAL Initiative®) was launched in 2018 and includes efforts to understand the impact of the opioid crisis on pregnant people and newborns. The Advancing Clinical Trials in Neonatal Opioid Withdrawal Syndrome (ACT NOW) Program is part of HEAL and combines the efforts of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Neonatal Research Network and the Institutional Development Award (IDeA) States Pediatric Clinical Trials Network (ISPCTN) to inform the clinical care of infants who are exposed to opioids in the womb. Three large-scale ACT NOW studies are currently ongoing: one study examines ways to soothe infants in withdrawal without medications, one study focuses on the best ways to provide medications to infants to treat withdrawal and taper them off over time, and one study is exploring the long-term effects and development of individuals born with neonatal opioid withdrawal syndrome (NOWS). HEAL is also supporting future studies that will begin in 2022 to address scientific and knowledge gaps in the clinical management of infants exposed to opioids *in utero*.

Another large study partially funded through HEAL and led by the National Institute on Drug Abuse (NIDA), the HEALthy Brain and Child Development Study (HBCD), is designed to elucidate the long-term effects of perinatal exposure to opioids on infant and child development. HBCD will follow a large cohort of pregnant women and their children from regions of the country significantly affected by the opioid crisis. The study will collect information beginning at birth and continuing through early childhood, including structural and functional brain imaging; physical measures; medical history; family history; biospecimens; and social, emotional, and cognitive development. Knowledge gained from this research will be used to better understand and ultimately prevent or attenuate the harms of prenatal and postnatal exposure to drugs or other adverse environmental conditions, including risk for early substance use, mental disorders, and other behavioral and developmental problems. It will also identify resilience factors that may mitigate some of these adverse outcomes.

NIDA also funds a large range of research projects on the mechanisms and consequences of prenatal drug exposure, including studies on cellular, molecular, and developmental outcomes; optimizing substance use disorder treatment for the mother-infant dyad; clinical markers and screening tools to detect neonatal abstinence syndrome (NAS)/NOWS; novel treatments for NAS/NOWS; and parenting interventions for at-risk mothers. NIDA-funded research has led to the development of the Prapela stochastic vibrotactile stimulation (SVS) hospital bassinet pad, which provides soothing vibrations and is used as adjunctive therapy in newborns with prenatal opioid exposure. Prapela has received Breakthrough Device designation from the U.S. Food and Drug Administration (FDA) for this therapy.

NIH research is advancing our understanding of the neonatal opioid exposure problem and discovering new ways to treat it. Recent ACT NOW work on infants with NOWS investigated treatment alternatives when first-line opioid therapy is ineffective. Phenobarbital and clonidine are typically used as secondary treatments for NOWS. The researchers found that babies treated with phenobarbital have a shorter length of hospital stay and shorter morphine treatment than babies treated with clonidine but are discharged from the hospital more often on secondary medication. Although further studies are needed to understand if the benefit of shorter hospital stays and morphine treatments outweigh the potential neurodevelopmental consequences of phenobarbital use in infants with NOWS, this study is an important step in improving understanding of optimal care for newborns exposed to opioids.

### ***Rare Cancer***

**Question:** Rare cancers account for 380 of 400 distinct forms of cancer and almost 1/3 of all diagnoses and include all pediatric cancers. A recent analysis showed that 80 percent of all patients who lacked an FDA-targeted therapy were rare cancer patients. In addition, of the 3,994 clinical trials in phases 1, 2, and 3 from January 1, 2012 to January 1, 2017, almost 75 percent did not include a rare cancer by name. While rare cancer affects every population, translational research and commercial drug development has traditionally neglected small patient populations. Each subtype of cancer requires a targeted therapy to save a life or to significantly improve lifespan.

- What is NIH's plan to ensure there is adequate investment in treatments for rare cancer patients?

### **NIH Response:**

The National Institutes of Health (NIH) remains committed to supporting research to advance the understanding of all cancers, including rare cancers, and to inform the development of targeted cancer therapies for rare cancers and rare subtypes of cancers, including pediatric cancers (all types and subtypes of pediatric cancers are considered "rare" by definition).

The cancer research community – thanks to NIH-supported developments in understanding the specific genes, proteins, and other unique molecular characteristics driving certain cancer

subtypes – continues to recognize that cancer is made up of a collection of hundreds, if not thousands, of subtypes defined by these characteristics. As a result of National Cancer Institute (NCI)-supported efforts and other relevant research, “cancer” is increasingly becoming a collection of rare cancer subtypes.

This evolved understanding of cancer is reflected in NCI’s current clinical trials portfolio and investments in translational and basic research, including several initiatives in the intramural Center for Cancer Research (CCR).

Increasingly, clinical trials are examining targeted therapies based on molecular subtypes. For example, NCI’s National Clinical Trials Network (NCTN) is currently supporting trials assessing therapies to treat gliomas with certain genetic alterations ([www.clinicaltrials.gov/ct2/show/NCT00887146](http://www.clinicaltrials.gov/ct2/show/NCT00887146)) and pancreatic cancers with specific gene alterations ([www.clinicaltrials.gov/ct2/show/NCT04858334](http://www.clinicaltrials.gov/ct2/show/NCT04858334); [www.clinicaltrials.gov/ct2/show/NCT04548752](http://www.clinicaltrials.gov/ct2/show/NCT04548752)). NCI also supports trials that are dedicated to patients with rare tumors, including the NCTN-supported DART (Dual Anti-CTLA-4 and Anti-PD1-Blockade in Rare Tumors) Trial ([www.clinicaltrials.gov/ct2/show/NCT02834013](http://www.clinicaltrials.gov/ct2/show/NCT02834013)) and the Rapid Analysis and Response Evaluation of Combination Anti-Neoplastic Agents in Rare Tumors (RARE CANCER) Trial ([www.clinicaltrials.gov/ct2/show/NCT04449549](http://www.clinicaltrials.gov/ct2/show/NCT04449549)), which is supported by NCI’s Experimental Therapeutics Clinical Trials Network.

To ensure that researchers have a strong pipeline of therapy candidates to consider for use in clinical trials, NCI supports several initiatives to support the preclinical stage of development of therapeutics to treat rare cancers, including the NCI Experimental Therapeutics (NeXT) Program and the Pediatric Preclinical Testing Consortium (PPTC). The mission of NeXT is to advance clinical practice and bring improved therapies to patients with cancer by supporting the most promising new drug discovery and development projects. The PPTC addresses key challenges associated with the development of new therapies for children with cancer by developing reliable preclinical testing data for pediatric drug candidates that can be used to inform new agent prioritization decisions.

The first step in identifying new therapeutic targets, however, is elucidating the basic biological mechanisms that give rise to cancers. To further these research efforts, NCI supports the development of resources for broad use across the cancer research community. These resources include cell lines, organoid models, patient derived xenograft (PDX) models, biospecimens, and other biological samples. NCI makes drug information summaries available on its website, along with extensive cancer treatment summaries. Additional resources include the Developmental Therapeutics Program, the National Clinical Trials Network (NCTN) Navigator, Patient-Derived Xenograft (PDX) Centers, PDX Finder, the NCI Mouse Repository, and the Physician Data Query (PDQ) Database. A more extensive list is available at [www.cancer.gov/research/resources/](http://www.cancer.gov/research/resources/).

The Rare Tumor Patient Engagement Network, launched in fiscal year (FY) 2018 and part of NCI’s CCR, leverages the resources of the NCI intramural research program and the NIH Clinical Center to bring together investigators, patients, and advocacy groups to study rare

tumors. Under the umbrella of this effort, NCI launched the My Pediatric, Adolescent, and Adult Rare Tumor (MyPART) Network, a collaboration of scientists, patients, family members, advocates and healthcare providers to find treatments for rare cancers. The MyPART Network collects samples like blood, saliva, and archived biopsy tissue from people with rare solid tumors as part of the Natural History Study of Rare Solid Tumors. The purpose of the study is to engage rare tumor patients and their families in the research process, study how rare tumors grow, track participants' health history over a long period of time, share data with other scientists, build new ways of testing new treatments, and design new clinical trials for rare cancers. MyPART scientists also hold clinics on rare tumors to facilitate collaborations between researchers, patients, and advocacy organizations; to date, MyPART has hosted clinics on chordomas, SDH-deficient gastrointestinal stromal tumors, and medullary thyroid cancer, and more clinics are in the planning stages. Additionally, the NCI Comprehensive Oncology Network Evaluating Rare CNS Tumors (NCI-CONNECT) program aims to advance the understanding of rare adult central nervous system (CNS) cancers by establishing and fostering patient-advocacy-provider partnerships and networks to improve approaches to care and treatment; seven clinical studies and trials are currently open through NCI-CONNECT ([www.cancer.gov/rare-brain-spine-tumor/refer-participate/clinical-studies](http://www.cancer.gov/rare-brain-spine-tumor/refer-participate/clinical-studies)).

Because of these and similar investments, the U.S. Food and Drug Administration (FDA) has approved a number of therapies in recent years for patients with rare cancer subtypes and related conditions. For example, in May 2021, the FDA granted accelerated approval to sotorasib (Lumakras) for patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with alterations in the *KRAS G12-C* gene, a mutation which is present in only 13.8 percent of NSCLC patients ([ascopost.com/news/january-2021/prevalence-of-kras-g12c-somatic-mutations-by-cancer-type-race-and-sex/](https://ascopost.com/news/january-2021/prevalence-of-kras-g12c-somatic-mutations-by-cancer-type-race-and-sex/)). Similarly, the FDA approved selumetinib (Koselugo) in 2020 for the rare tumor condition neurofibromatosis type 1, in patients over the age of two, as the first approved treatment for this condition. In 2018, the FDA granted accelerated approval to larotrectinib (Vitrakvi) for adult and pediatric patients with solid tumors with a neurotrophic receptor tyrosine kinase (NTRK) gene fusion. NTRK gene fusions are prevalent in nearly all cases of certain rare cancer subtypes, including secretory carcinoma of the breast or salivary gland and infantile fibrosarcoma; they have also been observed in some patients with more common types of cancer, such as glioma, melanoma, and carcinomas of the thyroid, lung, and colon ([www.ncbi.nlm.nih.gov/pmc/articles/PMC6859817/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6859817/)).

NIH will continue to support research efforts that reflect the scientific understanding of the many subtypes of cancers, including work that will enable the development of therapies for rare tumor subtypes.

**Submitted by Rep. John Moolenaar**

***Additional Research on Psychedelic Drugs***

I recently read articles about the potential therapeutic benefits of certain psychedelic drugs, such as psilocybin, MDMA, and ketamine, in the treatment of severe depression and post-traumatic stress disorder. Traditional pharmacological and psycho-analytical treatments are helpful, but some patients are not responsive. Recent research into alternative treatments – including psychedelic drugs – has shown promise in treating chronic and treatment-resistant mental health disorders when traditional treatments have failed.

Questions (for Dr. Volkow):

- Despite the common stigma associated with these drugs, could you please share your thoughts on the possible benefits of expanding research into these drugs?

**NIH Response:**

The National Institute of Mental Health (NIMH) supports the development and testing of therapeutic interventions for mental illnesses. This includes – when conventional interventions fail – the use of dissociative drugs such as ketamine and psychedelic drugs such as psilocybin. For example, the dissociative anesthetic ketamine<sup>32</sup> has recently emerged as an effective fast-acting antidepressant. The NIMH Director’s Message,<sup>33</sup> “New Hope for Treatment-Resistant Depression: Guessing Right on Ketamine,” describes the role of NIMH and other researchers in the development and U.S. Food and Drug Administration (FDA) approval of esketamine – a purified form of ketamine – for treatment-resistant depression.

- Has NIH reviewed research in the area of alternative treatments, including psychedelics, and if so, what conclusions has the agency drawn from this research?

**NIH Response:**

The National Institutes of Health (NIH) continuously reviews research in the area of alternative treatments, including psychedelics for mental illnesses and substance use disorders. Psychedelic drugs hold promise as potential therapeutics, although additional research is needed to examine their efficacy and safety, including following repeated exposures and potential interactions with concurrent treatments. In 2022, the National Institute of Mental Health (NIMH), the National Institute on Drug Abuse (NIDA), and the National Institute on Alcohol Abuse and Alcoholism (NIAAA) will host a scientific workshop to consider hallucinogens, psychedelics, and entactogens (a category of drugs that affect empathy or sympathy) as potential medications for the treatment of serious mental illnesses and substance use disorders. The workshop will emphasize gaps and challenges of

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<sup>32</sup> [pubmed.ncbi.nlm.nih.gov/27839782/](https://pubmed.ncbi.nlm.nih.gov/27839782/)

<sup>33</sup> [www.nimh.nih.gov/about/director/messages/2019/new-hope-for-treatment-resistant-depression-guessing-right-on-ketamine](https://www.nimh.nih.gov/about/director/messages/2019/new-hope-for-treatment-resistant-depression-guessing-right-on-ketamine)

conducting psychedelic drugs research, what has been learned to date, and optimizing future study designs.

- Has NIH received any applications for research grants for psychedelics, and if so, have they approved any?

**NIH Response:**

The National Institutes of Health (NIH) has funded several research projects involving therapeutic applications of psychedelic drugs. For example, within the National Institute of Mental Health (NIMH) Intramural Research Program, Dr. Carlos Zarate is conducting clinical trials<sup>34</sup> to better understand how ketamine rapidly reduces depressive symptoms in people with treatment-resistant major depressive disorder. Other NIMH-funded researchers are examining<sup>35</sup> the mechanisms underlying the antidepressant effects of psychedelic drugs in an effort to develop novel, non-hallucinogenic treatment strategies that are both safer and more effective than existing treatment options. The National Institute on Drug Abuse (NIDA) also supports research on psychedelics, including a clinical trial<sup>36</sup> which aims to assess the efficacy of ketamine in combination with behavioral therapy for the treatment of cocaine use disorders, as well as a trial<sup>37</sup> to compare the efficacy of the psychedelic drug psilocybin to the nicotine patch for smoking cessation. Additionally, a privately funded clinical trial<sup>38</sup> is assessing the potential efficacy of the psychedelic drug psilocybin for the treatment of obsessive-compulsive disorder. While the NIH is not directly funding this trial, NIMH does support the trial's principal investigator through a Mentored Patient-Oriented Career Development Award.<sup>39</sup>

- If they haven't approved any, what are the reasons for passing on the research opportunity?

**NIH Response:**

The National Institutes of Health (NIH) has approved research projects on the potential therapeutic effects of psychedelic drugs. For example, within the National Institute of Mental Health (NIMH) Intramural Research Program, Dr. Carlos Zarate is conducting clinical trials<sup>40</sup> to better understand how ketamine rapidly reduces depressive symptoms in people with treatment-resistant major depressive disorder. Other NIMH-funded researchers are examining<sup>41</sup> the mechanisms underlying the antidepressant effects of psychedelic drugs in an effort to develop novel, non-hallucinogenic treatment strategies that are both safer and more effective than existing treatment options. The National Institute on Drug Abuse

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<sup>34</sup> [clinicaltrials.gov/ct2/show/NCT03065335](https://clinicaltrials.gov/ct2/show/NCT03065335)

<sup>35</sup> [reporter.nih.gov/project-details/10003396](https://reporter.nih.gov/project-details/10003396)

<sup>36</sup> [reporter.nih.gov/project-details/9922890](https://reporter.nih.gov/project-details/9922890)

<sup>37</sup> [reporter.nih.gov/project-details/10187739](https://reporter.nih.gov/project-details/10187739)

<sup>38</sup> [clinicaltrials.gov/ct2/show/NCT03356483](https://clinicaltrials.gov/ct2/show/NCT03356483)

<sup>39</sup> [reporter.nih.gov/project-details/10127338](https://reporter.nih.gov/project-details/10127338)

<sup>40</sup> [clinicaltrials.gov/ct2/show/NCT03065335](https://clinicaltrials.gov/ct2/show/NCT03065335)

<sup>41</sup> [reporter.nih.gov/project-details/10003396](https://reporter.nih.gov/project-details/10003396)

(NIDA) also supports research on psychedelics, including a clinical trial<sup>42</sup> which aims to assess the efficacy of ketamine in combination with behavioral therapy for the treatment of cocaine use disorders, as well as a trial<sup>43</sup> to compare the efficacy of the psychedelic drug psilocybin to the nicotine patch for smoking cessation. Additionally, a privately funded clinical trial<sup>44</sup> is assessing the potential efficacy of the psychedelic drug psilocybin for the treatment of obsessive-compulsive disorder. While the NIH is not directly funding this trial, NIMH does support<sup>45</sup> the trial's principal investigator through a Mentored Patient-Oriented Career Development Award.

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<sup>42</sup> [reporter.nih.gov/project-details/9922890](https://reporter.nih.gov/project-details/9922890)

<sup>43</sup> [reporter.nih.gov/project-details/10187739](https://reporter.nih.gov/project-details/10187739)

<sup>44</sup> [clinicaltrials.gov/ct2/show/NCT03356483](https://clinicaltrials.gov/ct2/show/NCT03356483)

<sup>45</sup> [reporter.nih.gov/project-details/10127338](https://reporter.nih.gov/project-details/10127338)



TUESDAY, MAY 26, 2021.

**FISCAL YEAR 2022 BUDGET REQUEST FOR THE  
CENTERS FOR DISEASE CONTROL AND PREVENTION**

**WITNESSES**

**ROCHELLE WALENSKY, M.D., DIRECTOR, CENTERS FOR DISEASE CONTROL AND PREVENTION**

**ANNE SCHUCHAT, M.D., PRINCIPAL DEPUTY DIRECTOR, CENTERS FOR DISEASE CONTROL AND PREVENTION**

The CHAIR. This hearing will come to order.

As this hearing is fully virtual, we must address a few house-keeping matters.

For today's meeting, the chair or staff designated by the chair may mute participants' microphone when they are not under recognition, for the purposes of eliminating inadvertent background noise.

Members are responsible for muting and unmuting themselves. If I notice that you have not unmuted yourself, I will ask you if you would like the staff to unmute you. If you indicate approval by nodding, staff will unmute your microphone.

I remind all members and witnesses that the 5-minute clock still applies. If there is a technology issue, we will move to the next member until the issue is resolved, and you will retain the balance of your time.

You will notice a clock on your screen that will show how much time is remaining. At 1 minute remaining, the clock will turn yellow. At 30 seconds remaining, I will gently tap the gavel to remind members that their time has almost expired. When your time has expired, the clock will turn red and I will begin to recognize the next member.

In terms of the speaking order, we will begin with the chair and ranking member. Then, members present at the time the hearing is called to order will be recognized in order of seniority; and, finally, members not present at the time the hearing is called to order.

Finally, House rules require me to remind you that we have set up an email address to which members can send anything they wish to submit in writing at any of our hearings or markups. That email address has been provided in advance to your staff.

With that, I would want to acknowledge Congressman Harris, who is serving as ranking member today for this hearing in Congressman Cole's absence. And I also want to thank all of our colleagues for joining.

I am pleased to have the Centers for Disease Control and Prevention leadership back before the subcommittee to discuss the current state of the pandemic and our Nation's response and the President's budget request for fiscal year 2022 for the CDC.

On February 23, this subcommittee held a roundtable session with CDC focused on the COVID-19 response, and, a day later, we held a hearing focused on public health infrastructure.

Since that roundtable and hearing in February, our Nation's response to COVID-19 has made significant advancements. Vaccines are now widely available. One vaccine is now approved for those age 12 and above. Nearly 300 million vaccine doses have been administered, including nearly 4 million in my home State of Connecticut.

Last week, we heard from the Yale New Haven Health System that they are now treating a, and I quote, "staggeringly small" number of COVID patients. This is a tremendous accomplishment. Our public health workers are finally able to sleep again. Our families are finally breathing a sigh of relief. And our workforce and our economy are beginning to rebound.

But the messages from the public health infrastructure hearing in February were clear. COVID-19 exposed numerous realities in our Nation, including that our Nation's public health infrastructure is extremely fragile.

Many health departments are still using fax machines or doing data entry by hand. Information about patients' names, sex, or pregnancy status are not being shared across departments. Health workers are leaving the field in droves, while others need workforce development. And our research labs are struggling to find the equipment, capacity, and trained workforce they need.

But, now, communities are realizing that our public health partners are essential, not only for infectious diseases but for health promotion and protection to keep our communities healthy and functioning. Our Nation's public health system can no longer only get attention during a crisis. We must invest in the public health workforce, laboratories, and data modernization, not just to respond to the pandemic but every year.

After this pandemic is over, our public health agencies cannot go back to where they were. We need to meet this moment and build a public health architecture to move our public health partners and workforce forward. Today's hearing is the next step in turning those recommendations into action.

While we will not receive the details of the President's budget until later this week, we know from the budget blueprint that the administration is requesting \$8,700,000,000, an increase of \$1,600,000,000 over 2021 enacted, for the CDC. The administration has described this request as, and I quote, "the largest increase in budget authority for CDC in nearly two decades."

But, while this is a very welcome increase, I think in general we need to consider increasing investments for the CDC not just this year but every year. As I have said many times, one-time investments do not ensure the CDC and our public health departments are ready to address chronic challenges.

And we need to ensure our public health infrastructure is ready to address the challenges or pandemics of the future. This COVID-19 pandemic has only further underscored the need to view public health infrastructure as a fundamental service, not just something we fund when the need arises. The tide has turned. We need to start providing funding to address core public health activities.

While I look forward to receiving detailed requests for CDC, the programs highlighted to receive increases in the summary released in April are very welcome: maternal mortality prevention, firearm injury and mortality prevention research, climate and health, social determinants of health, and the establishment of a new community-based violence intervention program.

In terms of gun violence research, I am particularly interested in getting a progress report. I know it may be too early, but I hope that you can let us know a little more about the status of gun violence research and what we have learned.

In terms of maternal mortality prevention, I also want to say that I am pleased to see increased investments in research on maternal health to address the crisis of maternal mortality in the U.S. We absolutely need to make this a nationwide effort. Not one more mother should die just for participating in the miracle of birth.

I also think the increased funding for research on how to reduce racial and ethnic disparities in maternal health outcomes and improving maternal mental health is particularly crucial.

I might add that, 2 weeks ago, the CDC made a significant update to its guidance: that fully vaccinated people no longer need to wear a mask or physically distance in most situations.

Dr. Walensky committed to leading the CDC with science, and I know that we will have a lot of questions about the current scientific evidence that led to this updated guidance and the subsequent guidance that we are all awaiting to be updated by CDC.

I know that many people I have spoken to are still uncomfortable with this change and are not confident that being around people who are unmasked is safe. There is still a lot of uncertainty about the nuances that may be implied in such guidance.

Throughout this pandemic, CDC has been in the unenviable position of making black and white recommendations in a world of gray areas. So I think it will be helpful to drill down on what this guidance means and how we can continue to restore public confidence in such guidelines. That is why I greatly look forward to today's discussion.

Now, let me turn to my colleague, Congressman Harris, for any opening remarks that he may have.

Mr. HARRIS. Thank you very much, Madam Chair.

And good morning, Dr. Walensky. Thank you for coming before the subcommittee this morning.

Before I begin, I want to recognize the outstanding work and careers of Drs. Anne Schuchat and Nancy Messonnier, two longtime CDC physicians who have both recently announced their departures. I want to thank both of these remarkable scientists for their public service, dedication, and commitment to public health, especially during the COVID pandemic. You will both be missed.

Just over 14 months since the COVID pandemic began, it is finally winding down in America. I think it is worth recognizing once again the stunning success that rapidly bringing a COVID-19 vaccine to market has had on the trajectory of this disease in America.

The COVID-19 vaccines are the most quickly developed vaccines in history, thanks not only to the skill of researchers at Pfizer, Moderna, and other manufacturers but also due to the work of Operation Warp Speed under the previous administration. Operation

Warp Speed set our country up for the outstanding results of our current vaccination efforts.

It has been a pleasure for me personally to lend a hand to help get Marylanders vaccinated, and I continue to encourage to get everyone vaccinated as soon as they can. The vaccines are relatively safe and effective and are enabling us to resume our normal lives quickly.

On that note, I was glad to see that the CDC finally began to follow the science and recognize that vaccinated individuals can safely resume activities. Studies have shown for months that vaccines are effective and that outdoor transmission is almost non-existent.

I continue to question why the CDC resisted making these statements for so long, why many of our schools continue to be closed, why the mask mandate continues in the House of Representatives, and why children at outdoor camps this summer need to wear a mask.

One wonders whether pressure from teachers' unions and the need to distract from other difficulties facing our Nation, such as growing inflation, spiking gasoline prices, renewed conflict in the Middle East, have influenced this public health guidance on schools. I certainly hope this is not the case, but the timing and information about the influence that teachers' unions had on CDC guidance are troubling.

A key part of our transition back to normalcy will rely on fully reopening our schools. Census data shows that 50,000,000 working Americans have children who are school-age or younger. For many of these individuals, schools are the primary form of childcare. As such, it is imperative that all schools fully reopen immediately, not only so parents are not forced to choose between working and caring for their children but also so that the children can continue learning in the best educational environment.

Children with disabilities and those without as many resources at home have been robbed of over a year of academic, social, and emotional growth during this pandemic. But the science is clear: We need to bring these children back into the classroom now.

These are important issues to discuss, and I am sure there will be questions about them this morning, but let me briefly touch on the fiscal year 2022 budget request before I conclude my remarks.

The fiscal year 2022 request contains the largest budget authority increase in CDC in nearly 20 years. You are asking for funding to enhance State and local public health infrastructure as well as to build international capacity to detect and respond to emerging global biological threats.

I support many of these efforts. As an obstetric anesthesiologist, for instance, I especially support the focus on reducing maternal mortality and morbidity. But I do question the magnitude of these increase in a single year, especially when overlaid on top of the billions of dollars provided in emergency COVID relief bills last year.

I also question whether some of the funding items highlighted in your request are outside of CDC's core mission. For example, the budget will request double the amount of funding for firearm prevention research.

You are also asking for \$110,000,000 for CDC's Climate and Health Program, a 1,000-percent increase, to, quote, "identify potential health effects associated with climate change and implement health adaptation plans."

Are these kind of activities in the same priority category as combating COVID or other chronic diseases that threaten our most vulnerable populations or reducing antibiotic resistance? I would argue that they are not and that we should focus our CDC resources on communicable and chronic diseases rather than on controversial, politically charged activities.

I look forward to the hearing this morning, and I yield back the balance of my time.

The CHAIR. With that, we would like to again welcome and introduce our witnesses: Dr. Rochelle Walensky, Director, Centers for Disease Control and Prevention.

Good morning and welcome, Dr. Walensky. And many, many, many thanks for the outstanding work that you have been doing and really using science as your guide, particularly with regard to COVID and the manner in which we should proceed. And we are grateful for that guidance and, really, returning the CDC to, really, its former past in being drivers of science and letting the CDC, and not politics, engage in the direction that we take a pandemic or any other illness.

Dr. Anne Schuchat, Principal Deputy Director, Centers for Disease Control and Prevention.

And as my colleague has mentioned, you recently announced your plans to retire, Dr. Schuchat, after 33 years at the CDC. I say thank you to you for your dedication, for your public service. We have been many times—whether it was Ebola or whether it was the lead poisoning of our children in Michigan and other areas, you have had a stellar career. And we are delighted to have you once again before this subcommittee.

And, Dr. Walensky, your full written testimony will be included in the record. You are now recognized for 5 minutes for your opening statement.

Dr. WALENSKY. Good morning. Thank you very much. Good morning, Chairwoman DeLauro, Dr. Harris, and distinguished members of the committee. Thank you for your support of CDC.

I am here today, as you note, with Dr. Anne Schuchat, CDC's Principal Deputy Director. I have enormous gratitude for Dr. Schuchat's leadership and contributions over three decades as well as during this very challenging time for our country and for her rock-solid support of me in my transition into this role.

Anne embodies selfless public service, the pinnacle of scientific and intellectual standards, and has given her heart to our agency and to the public health community. I will be forever grateful that I had the opportunity to work with Anne, even if just during this brief period of time.

The COVID-19 pandemic threw the United States and the world into a health, economic, and humanitarian crisis. As the crisis unfolded, it put a spotlight on the fragility of our public health infrastructure. It illuminated great disparities in health outcomes by race and ethnicity, reminding us that, thus far, we have failed to

address the systemic racism that results in poorer health for people of color in the United States.

I am committed to working with you, the administration, and our public health partners to ensure that every lesson from this horrible crisis is used to build a better, stronger, healthier America. I also commit to using our public health expertise and experience, in partnership with the global community, to move the world into a safer, healthier future.

CDC's fiscal year 2022 discretionary budget request of \$8,700,000,000 is an increase, as noted, of \$1,600,000,000 over fiscal year 2021, the largest increase CDC has received in nearly 20 years.

The increase is focused on four critical areas: building public health infrastructure, reducing health disparities, using public health approaches to reduce violence, and defeating diseases and epidemics. These increases build on the investments made in the COVID-19 supplements and are an important first step in addressing deficits in the public health infrastructure.

COVID-19 not only exposed the vulnerability within the United States' public health infrastructure but also how underlying chronic conditions and lack of access to healthcare put too many Americans at great risk. Across the globe, we see billions of people without access to vaccines and medical care, which means that SARS-COV-2, its variants, and other infectious disease threats will continue to threaten us all.

Experts had warned for years that a pandemic of this scale was coming, and we must expect additional diseases to emerge. We need to ask ourselves, are we ready? We must have a strong infrastructure that can identify and detect outbreaks at their source and take quick action before they take hold.

Over the last 12 years, the United States has faced four significant emerging infectious diseases threats: the H1N1 influenza pandemic, Ebola, Zika, and now COVID-19. We are also confronting an overdose epidemic, a drug overdose epidemic, with nearly 500,000 people dying from an opioid-related overdose between 1999 and 2019. The increase continued in 2020 and appears to have accelerated during the COVID-19 pandemic.

These experiences show that public health emergencies are here to stay. Each of these threats demanded a rapid and unique response, but none resulted in the sustained public health improvements we need.

Long-term investments in public health infrastructure, flexible infrastructure, will save lives and avert economic losses caused by public health emergencies and chronic public health problems.

The fiscal year 2022 request makes initial investments to continue public health data modernization, build the public health workforce, enhance global health security, and strengthen our immunization infrastructure.

In addition, we are requesting funds to help States and communities be climate-ready and prepared to confront new health risks, such as those associated with vector-borne diseases.

The fiscal year 2022 request also makes specific investments in programs that work to improve health equity, such as maternal mortality review committees.

With new resources outlined in this request, CDC will also significantly expand efforts to address the social determinants of health. Proposed increases will address public health problems that have been exacerbated by the pandemic, such as opioid, injuries and violence, HIV, and sexually transmitted infections.

We at CDC are grateful for your support and look forward to working together to build a sustainable, resilient public health system that can respond effectively to emerging threats and meet the public health needs of every American. We will work tirelessly to ensure the health of this Nation and the world.

Thank you. Dr. Schuchat and I very much look forward to your questions.

[The information follows:]

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TESTIMONY

OF

ROCHELLE P. WALENSKY, M.D., M.P.H.

DIRECTOR

AND

ANNE SCHUCHAT, M.D.

PRINCIPAL DEPUTY DIRECTOR

CENTERS FOR DISEASE CONTROL AND PREVENTION

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

UNITED STATES HOUSE APPROPRIATIONS SUBCOMMITTEE ON  
LABOR, HEALTH AND HUMAN SERVICES, EDUCATION, AND RELATED  
AGENCIES

FY 2022 BUDGET REQUEST FOR THE CENTERS FOR DISEASE CONTROL AND  
PREVENTION

MAY 26, 2021



Chairwoman DeLauro, Ranking Member Cole, and distinguished members of the Committee, it is an honor to appear before you today to discuss how investments in the Centers for Disease Control and Prevention (CDC) are protecting American's health, now and in the future. I am grateful for this opportunity to address this committee, as well as for your long-standing and consistent leadership on issues of critical importance to the health of Americans, and the world.

It is my privilege to represent CDC at this hearing. CDC is America's health protection agency. For 75 years, CDC has been trusted to carry out its mission to protect America's safety, health, and security. Even during the unprecedented circumstances of the past year, CDC's scientific expertise, determination, selflessness, and innovation has helped the agency continue to advance its mission. We work 24/7 to prevent illness, save lives, and protect America from threats to our health, safety, and security. Addressing infectious diseases and pandemics, like COVID-19, is central to our mission. CDC's expertise lies in our ability to study emerging pathogens like SARS-CoV-2, to understand how they are transmitted, and to translate that knowledge into timely action to protect the public's health. CDC identifies and mitigates other causes of morbidity and mortality beyond infectious diseases, such as environmental and workplace hazards and intentional and unintentional injuries (such as those from falls, violence, or overdose). CDC promotes healthy behaviors, such as exercise and nutrition, to prevent chronic diseases such as diabetes and heart disease, and to prevent outcomes such as stroke. We promote healthy communities by increasing access to nutritious food and safe walking and green space. By deploying experts on the ground to support our state, Tribal, local, territorial and global partners, we translate science into implementing guidance that protects individuals, communities, and populations. In our work with other Federal agencies we ensure the safe and appropriate use

of medical countermeasures, including vaccines, and collaborate with the academic and private sector to further our understanding of new diseases and problems that affect health.

The COVID-19 pandemic threw the United States and the world into a health, economic, and humanitarian crisis. As the crisis unfolded, it put a spotlight on pre-existing weaknesses and gaps that threaten the health of Americans. It brought into stark light the great disparities in health outcomes by race and ethnicity. We must acknowledge the long-standing and too often unstated impact that racism has on public health. The pandemic has also highlighted our frail public health infrastructure, and the way that frailty impacted our ability to respond at the necessary scale and speed.

Experts had warned for years that a pandemic of this scale was coming. Today, we know to expect additional novel and currently rare diseases to emerge and gain footing as a result of our changing climate, closer interaction with animals, and globalization. Over the last 12 years, the United States has faced four significant emerging infectious disease threats – the H1N1 influenza pandemic, Ebola, Zika, and COVID-19. These experiences show that public health emergencies and, specifically, infectious disease threats, are here to stay. While urgency demanded rapid and unique responses to each of these threats, none resulted in the sustained improvements needed in our nation’s public health infrastructure. This lack of robust public health infrastructure continues to present significant challenges in our ongoing fight against COVID-19. In fact, emergencies have resulted in the rapid build-up of infrastructure needed to address the emergency, then dissolution of that infrastructure, often leaving no sustainable infrastructure in place to address the next threat. This lack of robust public health infrastructure continues to present significant challenges in our ongoing fight to tackle COVID-19.

World-wide, billions of people do not and will not have immediate access to COVID-19 vaccines. Cases will continue to increase, and variant COVID-19 strains are likely to emerge, persist, and cause outbreaks. As this becomes more common, our public health system at home and abroad must be ready with highly sophisticated detection and sequencing, combined with a rapid response at the source. The unprecedented investments provided to CDC through COVID-19 supplemental appropriations have helped our efforts to control COVID-19, and will also go a long way toward addressing deficits in the core components of the public health infrastructure that has long been ignored. Our ability to respond to the next public health crisis will depend on whether we invest in a public health system that is highly functional on a day-to-day basis and pivots to meet new threats, rather than continue our partial defense, which ramps up in response to an urgent and often short-term event.

A resilient public health system can be realized with careful planning that builds on the gains made with COVID-19 emergency supplementals and incorporates lessons learned as a result of this crisis, including reliable, flexible funding. The FY 2022 Discretionary Budget Request for CDC and ATSDR includes a total funding request of \$8.7 billion, an increase of \$1.6 billion over FY 2021 Enacted. This is the largest increase in budget authority for CDC in nearly two decades and defends Americans' health in four ways: 1) building public health infrastructure, 2) reducing health disparities, 3) using public health approaches to reduce violence, and 4) defeating other diseases and epidemics.

First, building the public health infrastructure. CDC's FY 2022 request prioritizes foundational funding to rebuild the public health infrastructure needed to safeguard the Nation's health and economic security. Drawing on lessons learned, as well as the latest information and technologies, CDC will begin to address long-standing vulnerabilities in the U.S. public health

network by training a larger cadre of experts who can deploy and support public health efforts, and building capacity to detect and respond to emerging global biological threats.

Public health action is driven by data. Earlier improvements in our systems for collecting information after other public health emergencies, including Ebola and EVALI, facilitated exchange of health information, linking local, state, and federal public health systems with healthcare systems and the public. With investments in public health data modernization in the FYs 2020 and 2021 appropriations and the COVID-19 supplementals, CDC increased the scale and speed of these systems during the COVID-19 response to protect people who are at risk for severe illness (such as older Americans), those with chronic medical conditions, and those from racial and ethnic minorities. These advancements must be applied across the public health system and at all levels of government. The funds requested in FY 2022 will be used to continue building a modern disease surveillance system at CDC, which will catalyze a multi-sectoral, comprehensive, and cohesive approach to documenting evidence, using state-of-the-art technology and analytical tools. CDC will continue working diligently to ensure its research and data are of the highest quality and are disseminated nationally to inform decision-making throughout the public health system, while supporting advances in data systems at all levels.

The COVID-19 pandemic made clear the role that CDC labs and public health labs across the nation play in conducting critical surveillance and responding to outbreaks and emerging threats. CDC and state laboratories were required to flex and surge during peak periods of illness, far beyond routine clinical testing. In FY 2019, CDC was only able to meet 50% of state and local health departments' stated needs for epidemiology and laboratory capacity funding, with personnel support being the biggest unfunded need, followed by equipment and supplies. The FY 2022 request will foster innovation, collaboration with the clinical system, and a

commitment to quality. Improving technologies at the state and local levels would enable public health labs to quickly utilize and scale up essential laboratory analyses. In a post-COVID-19 world, investments to maintain and improve laboratories will help prevent the failures we experienced while trying to address COVID-19.

The U.S. needs a workforce of qualified public health professionals who will prepare for, respond to, and prevent public health crises. Physicians working for states often earn less than \$150,000 per year. This is after having taken on medical school debt of \$200,000 on average. The FY 2022 request includes an increase to build a diverse and culturally competent workforce who can rapidly develop innovative approaches in surveillance and detection, risk communications, laboratory science, data systems, and disease containment. With this funding, CDC will support critical training programs for public health professionals that develop strategic and systems thinking, data science, communication, and policy evaluation. Existing cooperative agreement mechanisms will be leveraged to support public health jobs that meet current needs and attract new personnel to work in underserved and rural areas.

Addressing gaps in capacity across levels of government to detect and respond to outbreaks while maintaining and surging in other problem areas requires investments to be disease-agnostic and flexible. With FY 2022 funding, CDC will provide support to health departments to meet national quality standards, conduct performance improvement activities, increase communication and collaboration across the public health system, and reshape health departments to meet changing conditions and needs. Funding will help health departments strengthen their abilities to effectively respond to a range of public health threats, such as COVID-19, and build capacities that do not currently exist.

COVID-19 is a sobering reminder that a disease threat anywhere is a disease threat everywhere. Or as stated by WHO: no one is safe unless everyone is safe. We cannot adequately protect American lives and the U.S. economy without addressing global disease threats wherever they may arise. CDC's strategic investments in global health security are critical to U.S. health security by building sustainable global capacity to prevent, detect, and respond to emerging infectious disease threats. CDC works in more than 60 countries on more than 150 projects and is a key implementing agency for the U.S. Government's leadership role in the Global Health Security Agenda. With additional resources requested in FY 2022, CDC will build on existing partnerships with Ministries of Health, public health agencies, infectious disease research institutions, and international organizations to strengthen global laboratory capacity for early disease detection, enhance disease surveillance for accurate data to drive decision making, and foster effective regional and global coordination.

Next, I'd like to talk about reducing health disparities. The disparities seen over the past year among communities of color were not a result of COVID-19. In fact, the pandemic illuminated inequities that have existed for generations and revealed a known, unaddressed, and serious public health threat: racism. The well-being of our entire nation will be compromised as long as we fail to address this.

Racism is not just discrimination against one group based on the color of their skin or their race or ethnicity, but the structural barriers that impact racial and ethnic groups differently to influence where a person lives, where they work, where their children play, and where they worship and gather in community. The social determinants of health (SDOH)—such as high-quality education, stable and fulfilling employment opportunities, safe and affordable housing, access to healthful foods, commercial tobacco-free policies, and safe green spaces for physical

activity—are critical drivers of health inequities in this country, and impact individuals living in urban, rural, and suburban areas. CDC is building the evidence-base for collaborative approaches to SDOH through community accelerator planning and expanding a network of community health workers to develop a sustainable infrastructure to improve health equity. CDC's FY 2022 budget request includes an increase of \$150 million to use a social determinants of health approach to improve health equity and health disparities in racial and ethnic minority communities and other disproportionately affected communities around the country.

This budget directly responds to health disparities recorded in our public health data. For example, about 700 women die each year in the U.S. as a result of pregnancy or delivery complications, and American Indian, Alaska Native, and Black women are two to three times more likely to die than White women. Data show that about 2/3 of these deaths may be preventable. Children from lower-income and racial and ethnic minority households experience a disparate, increased risk for lead exposure.

Achieving health equity is central to addressing the HIV epidemic. The U.S. government spends \$20 billion per year in direct health expenditures for HIV care and treatment. An estimated 1.2 million persons have HIV and approximately 15% are unaware they have it. With recent advancements in antiretroviral therapy and biomedical advancements in HIV prevention, such as pre-exposure prophylaxis (PrEP), along with effective care and treatment, we have the tools to end the HIV epidemic. An increased investment requested in FY 2022 for the Ending the HIV Epidemic (EHE) initiative will enable CDC to advance the four key strategies needed to end the epidemic in the 57 EHE focus jurisdictions. In addition, CDC will address health equity in the entire HIV prevention portfolio, test innovation in service delivery models to increase access to prevention services, use syndemic approaches to broaden reach to key populations and create

efficiencies, and strengthen engagement of grassroots community-based organizations in implementing EHE initiative.

Third, the budget request also addresses the public health epidemic of violence. We know too well how this epidemic permanently alters the lives of its victims and their families and puts enormous strain on our communities and local economies. Increases in CDC's FY 2022 budget request will help address violence through public health approaches, which include improving reporting systems that provide the data needed to understand and address violent deaths and injuries in the United States.

And fourth, we must defeat other diseases and epidemics. Just as racism underlies a number of public health issues, climate issues underlie a number of infectious diseases and have significant health impacts. Climate changes are associated with changes in the geographical range of mosquitos, ticks, and other disease vectors. Climate-related events impact a wide range of health outcomes. Some of the most significant climate-related events—such as heat waves, floods, droughts, and extreme storms—affect everyone. These climate events compromise our access to clean air, clean water, and a reliable food supply. In addition, climate events can impact the presence of allergens and vectors, like ticks and mosquitoes, and the subsequent health outcomes that can result from these changes in exposures. We know that a changing climate can intensify existing public health threats, and that new health threats will emerge: unequally distributed risks (age, economic resources, location), increased respiratory and cardiovascular disease, injuries and premature deaths related to extreme weather events, changing prevalence and geography of foodborne and waterborne illnesses and other infectious diseases, and threats to mental health as people feel less safe.



CDC works with states, cities, and tribes to apply the best climate science available, predicting health impacts, and preparing public health programs to protect their communities. To do this, CDC developed the Building Resilience Against Climate Effects (BRACE) framework to help communities prepare for the health effects of climate change by anticipating climate impacts, assessing vulnerabilities, projecting disease burden, assessing public health interventions, developing adaptation plans, and evaluating the impact and quality of activities. With the requested increase in FY 2022, we can further expand the Climate and Health Program by providing a larger number of health departments with technical assistance and funding and finding innovative ways to protect health via climate adaptations. As with every other public health threat, we will inform our effort by building and examining systems that collect data on conditions related to climate, including asthma and vector-borne diseases, and coordinate programs and communication that improve health outcomes.

The opioid epidemic has shattered families, claimed lives, and ravaged communities across the Nation—and the COVID-19 pandemic has only deepened this crisis. Addressing the current overdose epidemic remains a priority for CDC. The Administration’s strategy brings together surveillance, prevention, treatment, recovery, law enforcement, interdiction, and source-country efforts to address the continuum of challenges facing this country due to drug use. CDC’s role is to prevent drug-related harms and overdose deaths.

The additional funding requested in FY 2022 to address the opioid epidemic will enable CDC to provide more funding to all States, Territories, and select cities/counties. CDC will prioritize support to collect and report real-time, robust overdose mortality data and to move from data to action, building upon the work of the Overdose Data to Action (OD2A) program. To do so, CDC will partner with funded jurisdictions to implement surveillance strategies that

include contextual information alongside data, as well as increase surveillance capabilities for polysubstance use and emerging substance threats such as stimulants. The additional resources requested will enable CDC to support investments in prevention efforts for people put at highest risk, for example, supporting risk reduction and access to medications for opioid use disorder for people transitioning from alternate residence (jail/prison, treatment facility, homeless shelter). CDC will also address infectious disease consequences, such as viral hepatitis, of the opioid epidemic.

I look forward to working together to address both the immediate challenges ahead in our fight against COVID-19, as well as the weaknesses in the public health infrastructure that left our country vulnerable to this pandemic. We at CDC are grateful for your support. We will continue to work tirelessly to ensure the health of this nation and the world. Together, we can build a sustainable and resilient public health system that can respond effectively to emerging threats and also to ongoing public health needs of every American.

The CHAIR. Thank you very much, Dr. Walensky.

I also might add, before I get to my question, that when you spoke about the work done by CDC with the vaccine, et cetera, I also want to mention—because yesterday we had the NIH appear before the committee for their budget hearing. And it was remarkable that the achievements that you have made were—you know, this was possible not only by targeted investments in COVID research but, I believe, also—and I think that the subcommittee agreed yesterday on a bipartisan basis—also by the annual and the sustained investments in biomedical research made by this committee over the years, which was over \$650,000,000 in basic research on coronavirus that helped us to be able to move as rapidly as we were able to. And, again, thank you for your outstanding work in this area.

I have a question for you, Dr. Walensky, and I will also ask Dr. Schuchat to respond to it.

It is clear to me that our Nation's public health agencies cannot go from crisis to complacency to crisis. We can't think about public health agencies just during the crisis, about thinking about the infrastructure of our public health system.

In your opinion, what COVID-related lessons and response efforts need to be sustained post-pandemic that public health agencies, including CDC, as well as State and local health agencies, are better positioned every day to support the health of our communities?

When we did our hearing, our health partners testified about core needs—public health data, workforce, laboratory—that are not specific to one disease or activity. Do you agree?

Dr. WALENSKY. Thank you, Chairwoman DeLauro.

First, let me say congratulations to you and the State of Connecticut for all of your extraordinary work—

The CHAIR. Thank you. Thank you.

Dr. WALENSKY [continuing]. On getting the vaccine rolled out. You have been a beacon example. Thank you to you and the State. That has been extraordinary.

Maybe I will just jump off of where you started with this, which is the NIH, and just comment that what we are looking for in the CDC budget is something very similar to what has occurred with NIH, and that is long-term, longitudinal, sustainable increases.

And maybe I will just highlight that there is evidence that, once a scientific study has been published, that by the time it gets to the community, the core community, in the rural South, in the urban settings, that it can take up to 17 years before it gets from the scientific data to a guidance, to training doctors, to reaching people in hospitals, to then reaching people in the core community. It can take that long. And that is the work of what public health can do. And that is why we need the sustainable resources.

I think the buckets that you have just described are exactly where we need to be on what we have learned where we were fragile in the COVID-19 pandemic.

Our workforce. We need an upskilled, trained workforce that is diverse both in discipline and in background coming from the communities that they are going to serve. We know that, over the last decade, when we have had all of these infectious threats, that we

have lost over 60,000 public health jobs. We also know that about a quarter of our public health workforce is eligible to retire. So we now need a data-savvy, skilled workforce that works at State health departments, local health departments, and, in the communities, community health workers to reach the people that they serve.

We need to bolster our public health labs. When we started in this administration, we were doing less than 3,000 samples of genomic sequencing a week. We are now up to 35,000 samples a week. We didn't have the infrastructure in the lab to be able to bolster that.

And then, finally, as you note, the data modernization and the need—you mentioned the faxes, the personal data entry, the need to bolster our data to make sure it is interoperable across different health departments, across different States, and up to the CDC.

The CHAIR. Okay.

Dr. Schuchat, would you like to please comment? Thank you.

Dr. SCHUCHAT. Thank you so much. And thank you for your kind remarks.

Just to, of course, agree with Dr. Walensky about the priorities, I would just add that we live in a global world and that COVID has taught us that a threat anywhere is a threat everywhere.

We were not as prepared as we thought we were here. And we know that every Nation needs that capacity to prevent, detect, and respond adequately. And we need systems that can surge rapidly. And we need to work together on that.

I regret that I will be 33 years at CDC, leaving with a public health infrastructure that is not stronger than when I got here. When I look at the NIH and the enormous improvements in biomedical research capacity that we have seen, I wish that we have seen the same kind of strengthening of our public health capacity.

Because I think we have all seen that, regardless of the fantastic scientific breakthroughs, if we don't have that frontline workforce and we don't have a nimble and resilient system, if we don't have data systems that surge and are faster than the threats we are facing, that we are all vulnerable.

So I hope that the incredible investments in COVID will be extended for the other threats that are out there.

The CHAIR. Just a quick followup. We included in the emergency supplemental last year expediting the modernization, the data modernization initiative. Just very quickly, can you give us, you know, any kind of a progress update on the multiyear initiative?

Go ahead. Dr. Walensky.

Dr. WALENSKY. Sure.

You know, this has been something that we knew we needed to address early on. And we are now working across—so, for example, the electronic health records that we were able to do in COVID, we were able to bridge test results with electronic health records from Cerner and Epic to be able to gather more data in a HIPAA-compliant way.

So all of these systems have been bolstered very much. We have had to move quickly through the COVID-19 pandemic. But we really do need to work with our health centers, our public health

workforce, bioinformatics and information through the private sector. And all of that work is actively ongoing.

The CHAIR. Thank you.

My time has expired. So, Congressman Harris, please. Sorry I went over time. Go for it, Dr. Harris.

Mr. HARRIS. Thank you very much.

And, you know, one thing that is important is that the public have trust that science is behind decisions made by CDC and public officials.

So the first question I want to get out of the way quickly is that—Dr. Walensky, are you and Dr. Schuchat in the same room?

Dr. WALENSKY. We are.

Mr. HARRIS. You are. And neither of you have masks on.

So what I am going to ask you is—you know, if we were conducting this hearing in a House committee room, we would all have to wear masks, whether we were vaccinated or not, because that is the ruling of the Speaker. In fact, in the House Chamber, we have to wear masks.

I have a very simple question. Did the Speaker or the Attending Physician of the House consult with you or anyone else at CDC before coming up with that policy—a policy that, by the way, results in a fine of up to \$2,500 for someone who is not wearing a mask who has been vaccinated.

Did they consult with you?

Dr. WALENSKY. We put our mask on till about 2 weeks ago to—that spoke to the science about individual risks, and, in fact, those decisions have to be made locally. So our guidance was data-informed, scientific—

Mr. HARRIS. Did they consult with you before coming up with the House policy?

Dr. WALENSKY. We have been in contact with both the Capitol Physician as well as the Speaker's office.

Mr. HARRIS. So they consulted with you about this policy?

Dr. WALENSKY. There has been—we have been in dialogue—

Mr. HARRIS. That is a simple question. Before they came up with the policy, which is a new policy now, that 100 percent of people have to be vaccinated before anybody takes a mask off, did they consult with you about science behind that policy?

Dr. WALENSKY. The science that we put in our guidance is related to the science of individual risk. And then the decisions have to be made at the local level with data that we do not have access to.

Mr. HARRIS. Dr. Walensky, that is not responsive. And, you know, I am actually puzzled by why you are not—it is a simple “yes” or “no” answer. Did they consult with you?

This is why America doesn't trust public health officials. This is why America doesn't trust elected officials. Because I can't get a straight answer about whether the Speaker of the House and Attending Physician consulted about the latest change in policy, which is that 100 percent of Members and staff have to be vaccinated before anyone takes their mask off.

Let me turn to the problem with schools. Is it true that the teachers' unions helped drive the CDC policy on reopening schools?

Dr. WALENSKY. As a matter of practice within the CDC, we engage with many partner organizations related to any guidance that we have put out. So it—

Mr. HARRIS. Okay. So it is just coincidence that the wording of the guidance pretty closely mirrors some of the discovered communications between the teachers' union and CDC?

Dr. WALENSKY. We engage with many partners. I spoke to teachers, I spoke to parents, I spoke to many people before that guidance came out. And what became clear in some of those discussions is that there was a piece missing.

The teachers were asking for, what happens if we have a teacher who is immunosuppressed? How do we act if we have a teacher who is immunosuppressed or a family member of that teacher who is immunosuppressed?

That piece was missing from our original document. With the feedback, we were able to include science-based recommendations.

Mr. HARRIS. Okay.

Now, the other thing that—and, again, I appreciate we discussed at some length yesterday on the telephone the need for people who have had prior infections to be vaccinated with two vaccines, if they are receiving Pfizer or Moderna, despite the evidence that there is a—first of all, that there is a good T-cell response following natural infection, whether symptomatic or asymptomatic. That information has been out there for months. And a recent study by the Penn Institute of Immunology indicated that there is a very robust response after only one additional vaccine.

So, given that these are still experimental vaccines, these are under emergency-use authorization, would it be reasonable to begin looking at saying that people who have had disease should either have tests for antibodies or T cells or should only get one vaccine if they are in a two-vaccine regimen?

Dr. WALENSKY. Dr. Harris, I think you bring up one of the things that is going to be the Holy Grail of this, and that is, what are the correlates of protection, both in the T cells as well as the B cells?

As we had the pleasure of discussing the other day, we don't have great correlates of protection in either of these. And, in fact, we can easily measure antibody response. We don't even have a good measurement of T-cell response right now.

When we get those measurements that we can use in a large-scale public health sort of way—

Mr. HARRIS. So the Oxford—and I only have a few seconds left. The Oxford Immunotec test, which, unfortunately, FDA has put on the back shelf for evaluating for EUA but is licensed in England, is not a good test?

Dr. WALENSKY. I am saying it is not applicable that we can use now in a public health way to make a decision about whether somebody who is sitting in front of us should get vaccinated or not.

Mr. HARRIS. Sure.

Thank you. I yield back.

The CHAIR. Thank you.

I would just like to make a comment. I am looking at a document that is dated May 13, 2021, and this was a major speech made by the American Federation of Teachers president, Randi Weingarten, where she says, "There is no doubt: Schools must be open, in per-

son, 5 days a week, with the space and facilities to do so. We know that is how kids learn best and that prolonged isolation is harmful. Educators have yearned to be back in school with their students. They only ask for two things: a safe workplace during this pandemic and the resources they and their students need to succeed.”

With that, I am going to recognize Congresswoman Lee. But I am going to step away for a moment to pose a couple of questions to Secretary Mayorkas in the Homeland Security hearing, and Congresswoman Lee will take over the gavel while I am gone. I should be back in short order.

So, Congresswoman Lee, you are recognized.

Ms. LEE. Thank you very much, Madam Chair.

And thank you to Dr. Walensky for your testimony and also for your leadership in declaring that racism is a public health threat.

And also to Dr. Schuchat, thank you so much for your 30 years of service and your commitment to public health. We are going to miss you, but you have really made your mark. So thank you so much.

Let me ask Dr. Walensky, with regard to the whole issue of structural racism and public health—it is undeniable, so, again, thank you for the declaration.

We have to work together to ensure that our healthcare systems work to confront and dismantle the racist systems and practices that perpetuate racial disparities. And so Congresswoman Ayanna Pressley, Senator Warren, and myself, we introduced the Anti-Racism and Public Health Act, which calls for the development of a national center for anti-racism at the Centers for Disease Control and Prevention and also a law enforcement violence prevention within the National Center for Injury Prevention and Control at the CDC in coordination with the Department of Justice.

Now, the President has included \$100,000,000 for CDC to start a new community-based violence prevention—or violence intervention initiative. And so in what other ways are you going to ensure the interagency and interdepartmental collaborations and accountability to really begin to address and dismantle racism in public health? And is this \$100,000,000 appropriate to use to begin to establish some of these programs that we have laid out in our legislation?

Dr. WALENSKY. Thank you so much, Congressman Lee, and really to you for your extraordinary leadership in this area. As I think you know, I have history in my work in HIV, which is where this interest for me had started, and I know you share that interest as well.

As you know, about a month ago, we declared here at CDC racism as a serious public health threat. Through COVID-19, we very much saw that: 0.8 years of life lost for people who are White, 1.7 years of life lost for people who are Hispanic, and 2.9 years of life lost for people who are Black in this country due to COVID-19. Truly extraordinary years of life lost. And that has, you know, opened the door for us to be able to do that for everybody else to see what you and I have been seeing for years, that health is different for people of color in this country.

One of the things I charged my agency with, my center directors with, when we made this declaration is to say, yes, we have docu-

mented the problem in all sorts of different kinds of screening mechanisms and in all sorts of different care, we have documented that these are disparities in care; I want to now do something about it.

So I have asked each of my agency center directors to plan an intervention for the next year, a measurable intervention, that will show impact in how we can improve health in people of color in this country.

And among the areas where we are going to be using these resources is deep in these communities. It is among the reasons that we need community workers, to understand the impact of what is happening in those communities and understand how we can reach them.

And I really look forward to seeing what our center directors are planning and what they find.

Ms. LEE. Thank you.

And one thing I am working on, Dr. Walensky, is the issue of the lack of Black men in medicine and behavioral health professionals. And so anti-racism strategies have got to be integrated into all areas where we see shortages of people of color.

And so I am wondering, as you move forward on this, how are you looking at putting these strategies together, across the board, everywhere within your authority?

Dr. WALENSKY. You know, one of the things I think that is so important is that our workforce be diverse, both in their expertise as well as in their background and the communities they serve. They need to come from the communities they serve.

I had the great pleasure of being in rural Georgia last week talking to a rural community, and I said, "How are you doing at vaccination?" And they said, "Well, it didn't work when they sent in the National Guard." They trust the local firefighter, right? These communities trust the people who have been in the communities, from the communities.

I have seen that in working with community health workers in my own HIV work back in Boston. They trust the people from their community. It has to be at every single level of expertise.

Ms. LEE. Okay. Thank you.

And, finally—I have a few seconds left—let me just ask you as it relates to sterile syringes. We know it is the most effective intervention to prevent the spread of infectious diseases. And so how are those syringe service programs working? And how are we encouraging organizations, healthcare entities, to use this program, syringe service programs?

Dr. WALENSKY. You know, the opioid crisis is a real challenge. It had been a challenge before the pandemic. It continues to be a challenge, both with—and, in fact, was exacerbated by the pandemic, both in terms of infectious threats that are transmitted through injection use—and so, yes, we are working closely to embrace the sterile syringes under the context of the law and what we are able to do. And we are really looking forward to moving forward with you.

Ms. LEE. Thank you very much.

I guess our chair—I will yield back to you now, Chairwoman DeLauro. You made it back.



The CHAIR. Congresswoman Herrera Beutler.

Ms. HERRERA BEUTLER. Thank you, Madam Chair.

And thank you both for being here and for your service.

I think my question is for you, Dr. Walensky. And I think part of my challenge is, it is all based around how we are treating children in this pandemic.

You know, there is a large amount of discussion around school reopening, but I hear from parents in my parent whose children are being forced to quarantine for long periods of time beyond CDC guidance, which ultimately interrupts their learning.

And, in some cases, a medical provider is not allowed to clear a child to return to school. And throughout your guidance for school reopening, the CDC has encouraged students and parents to talk to their healthcare providers, but it seems like their opinions are being overlooked, which is hugely disappointing.

So, on one hand, I want to make sure that you are communicating, and I wanted to ask what you are doing to communicate down through the levels to the local level that can provide some of this guidance.

But then I think the broader observation that I have is, I do think we are getting so many mixed messages. It is very difficult to have one source of information. You know, I saw a story in The New York Times from a week or two ago that said that CDC's benchmark for outdoor transmission was about 10 percent, which, if you dig down on the science on that, it is really—leading doctors will say it is actually less than 1 percent. So to say 10 percent is not inaccurate; it is just really imprecise.

And so, when you have this kind of muddle of information flowing around, it causes some real challenges on how do we provide leadership in our communities with regard to what to do.

That brings me to the next point, which is masking in children. I brought this up yesterday. I think children have disproportionately borne the isolation burden throughout this whole pandemic, whether it is learning loss through school, interaction with one another, especially children in the younger grades who are learning to talk, who are learning to interact, whose social and emotional interaction is really what is at stake.

You know, I saw some remarks from—I am not going to say his last name right, so I am not going to try—a doctor from Stanford, but I can provide you his name—I just don't want to butcher it—citing studies from Sweden and the WHO, who recommend in The Wall Street Journal that we avoid masking kids up until at least age 11 because they are at low risk for infection and the very real hazard is stunting their development.

And yet our only recommendation at this point is, kids, young kids, you are going to have to continue to mask. As we are lifting this burden on everyone else, we are going to make you do it. We are even going to make you do it outside, where there isn't a single documented, you know, infection instance anywhere in the world from that casual outdoor interaction.

So I wanted you to speak to—because science, science, science is our base, right? That is what you said; that is what the chair said. I believe that. But the science doesn't show that children are at high risk. And a CDC study from last July shows that they are not

at high risk for spreading it either, when we are talking about, you know, about 2 to 7, 8, 9, right?

So why are we making the kids bear this burden?

Dr. WALENSKY. Thank you, Congressman.

First, maybe I will acknowledge two important things. One, I have three kids myself. One has been home all year. I understand the challenge. I deeply understand the challenge.

And maybe the second is the complexity of managing guidance and information and providing it to the public when it is changing and when it is evolving and when we are learning so much so quickly, and how we are able to evolve our guidance in the context of that.

And I think you are highlighting something that is really important. This is complex. And as we change things, things that we knew a year ago are different now because we have much more information and they continue to evolve.

I have always said schools should be the last place to close and the first place to open. And I very much still agree with that. I very much want those to be safe places. My own kids were home from camp last summer, and I want camps to be open this summer.

All of our guidance has highlighted it is better to be outside than inside. And what I really want in our camp guidance—and we are working through revising that guidance in the context of vaccination for 12- to 15-year-olds. My whole goal is to make sure that camps can remain open and that outbreaks don't occur.

Ms. HERRERA BEUTLER. But can I jump in on there, just because my time is running low? And I appreciate that.

Based on the science, children 0 to 4 are less than, I think it is, 1 percent or 1.3 percent of all infections. And so I guess part of me is saying—I get it, 12 and up, you can get a vaccination, but you can't vaccinate the younger kids. Yet they are at low risk for getting it. They are at even lower risk for hospitalization. They are at low risk for spreading it. So why are we making them mask? Because the science doesn't support that.

Dr. WALENSKY. There are still transmissions associated with young children. They have been vectors of transmission for older people. And—

Ms. HERRERA BEUTLER. What studies—that is the thing I need to know. Maybe you can provide that, because my time is up.

Dr. WALENSKY. I would be happy to do that.

Ms. HERRERA BEUTLER. Can you provide the studies for that? Because that is not readily available.

Dr. WALENSKY. Absolutely.

Ms. HERRERA BEUTLER. Thank you.

The CHAIR. Congressman Pocan.

Mr. POCAN. Thank you very much, Madam Chair.

And thank you both for being with us.

First, I just want to say, you know, I am very happy with the increase that you have. You have outlined many ways you are going to spend it. I guess my only regret, and this might be Barbara Lee's as well, is that the Pentagon increased budget alone is more than 50 percent than your total budget. For perspective, I think that is important for people to understand, given the biggest threat to this Nation in the last year was COVID-19.

Having said that, let me ask a couple questions, first about contact tracing. Is this a good time to really be very specific in our contact tracing efforts?

I know it was hard at moments last year to keep up. I think at one point we were doing one out of every five people is the best we could do in the State of Wisconsin. But now that you have far fewer people, is this something worth intensifying the efforts on to really help further eradicate its spread?

Dr. WALENSKY. Thank you, Congressman.

Contact tracing has always been a strategy for containment. We have used it in measles when we have fewer cases. And, in fact, it is hard to do contact tracing when you are in a mitigation strategy with hundreds of thousands of cases, as you exactly note. So, yes, I think now is a good time. With fewer cases, we are able to do so, we are able to isolate.

But I think one of the bigger things to mention is, who are those contact tracers? They are the community health workers. They are the people who are on the ground, the infrastructure we never had, that we couldn't deploy to do the contact tracing to begin with.

And that is what a sustainable public health infrastructure will be able to do. They will be able to be in the community, working on hypertension, childhood vaccinations, diabetes control, and then pivot quickly when you have an emerging threat.

So I believe our contact tracers should not only serve as contact tracers now but as vaccine navigators—they know their community—and, really, to promote both quarantine of people who are potential contacts but then vaccination.

Mr. POCAN. I don't want to put words into your mouth, but I would like to be able to pass on this information. So this would be a good time to make sure that we are thoroughly doing contact tracing with the limited cases that we now have?

Dr. WALENSKY. And I would emphasize, contact tracing with vaccination.

Mr. POCAN. Yes.

Dr. WALENSKY. Because those who have to quarantine are likely those who are not vaccinated.

Mr. POCAN. Gotcha. Thank you very much.

Second question is—I know that, you know, when you put out the new guidelines, it was a lot of new guidelines, ones for everybody.

And, last night, Secretary Walsh was in town, so I was out doing a few things in the community. And, based on your guidelines, I haven't been doing many things—I wasn't supposed to—in my district that previously I have.

But it seems like the change has been very—a lot of people are doing a behavior without masks and things, which is in many ways okay.

Are there things that, if you are vaccinated, that we should still not be doing right now, and if you are in a mixed crowd, that we should not be doing right now?

Dr. WALENSKY. Thank you.

You know, the guidelines that we put out for fully vaccinated people was really intended at the individual level. And I think

what we really need to understand is that the policies have to be locally driven.

What we know is that there are counties that still have less than 20 percent of people vaccinated and still greater than 100 per 100,000 cases of disease every 7 days.

And so this was the start, because, in fact, we needed people to recognize that this was important information, science-based information, to make those local policies. But the heterogeneity of both vaccine rollout and cases, I think, really needs to be taken into account here.

Mr. POCAN. So, for example, indoor situation but mixed. If you know at least a quarter of the people aren't vaccinated and you are within 2 feet of people in the size of the room, should you be wearing a mask?

Dr. WALENSKY. I would defer to the local policy. But I would say, if you need to make that decision yourself and you are vaccinated and you are not immunocompromised, it is not you that is at risk; it is the unvaccinated cohort.

Mr. POCAN. Gotcha.

And then a last question in the minutes left about sending vaccines abroad. You mentioned in your initial comments—I personally am trying not to do any international travel this year, just because I think, you know, the rest of the world is not as far as we are in vaccines.

But what should the U.S. be doing more to make sure—because we are never really going to be in the place we want to until we get people vaccinated across the world. What more should we be doing?

Dr. WALENSKY. I think, as Dr. Schuchat already noted, disease anywhere now is a threat to us here. And so we need to be assisting.

We have already put \$4,000,000,000 into COVAX—\$2,000,000,000 that has already been given and another \$2,000,000,000 that is going to be—80,000,000 doses of vaccine that we are hoping to get out before the end of June.

And we at CDC are going to be providing global support, technical support, how we do massive immunization campaigns, how we do vaccine safety. And we will be providing all that support.

Mr. POCAN. Great.

And just in the remaining 9 seconds, thank you. I know you have all put a lot of extra time in. It has been a pretty tremendous time in our history. I just want to say thank you.

And I yield back, Madam Chair.

Dr. WALENSKY. Thank you so much.

The CHAIR. Congressman Cline.

Mr. CLINE. Thank you, Madam Chair. I appreciate you having this hearing today.

I want to thank our witnesses and ask Director Walensky, in encouraging vaccinations—and I encourage people to get vaccinated—you mentioned that we need to be specific for each locality, each individual.

But suffice it to say that your recommendations include the idea that, if you are vaccinated, not only do you run a reduced risk of

contracting COVID but you have a reduced risk of transmitting COVID. Is that accurate?

Dr. WALENSKY. That is what emerging science is telling us, yes.

Mr. CLINE. Okay.

So, circling back to the ranking member's questioning, were you in contact with the Attending Physician, Dr. Monahan, as he developed this most recent policy announced by the Speaker, where 100-percent vaccination was encouraged? Were you in contact with the Attending Physician?

Dr. WALENSKY. We have been a resource for the Capitol Physician throughout this pandemic. I know our offices have been in contact with him. I can't tell you exactly the timing of that, in terms of when the last discussion was versus when the guidelines for the House came forward.

Mr. CLINE. Okay.

Were you in contact with his office as he developed recommendations for the Senate? Because the Physician also provided a recommendation to the Senators as well. Were you aware of that?

Dr. WALENSKY. Congressman, my reply to that would be the same. I know our office has been in contact, but I just couldn't tell you when our office was directly in contact with him and when his decisions for either the House or Senate occurred.

Mr. CLINE. And would it surprise you to learn that the Attending Physician issued a recommendation to the Senate that was substantially different than the recommendation to the House, in that the Senate was encouraged to proceed with normal business without masks being required, social distancing respected, but that 100-percent vaccination was not required in recommendations from the Attending Physician's Office to the Senate, but in the House it is somehow being mandated? Does that surprise you?

Dr. WALENSKY. Congressman, one of the things we have just mentioned is how complex these decisions are. In the case of evolving science, of course the Capitol Physician has much more information than I do about both the vaccination rates in each, the House and the Senate, as well as the medical records of people, as well as the average age and immunity durability. So I think he would be best equipped to make those decisions.

Mr. CLINE. Well, the Senators, on average, are older. The average age of the Senators is higher. And the science of the virus is not different in the Senate Chamber than it is in the House Chamber, correct?

Dr. WALENSKY. I just don't know the immunization rates of each of the House and Senate. And he would be equipped with that information that I don't have.

Mr. CLINE. Is it your opinion that American society should be 100-percent vaccinated before we open back up?

Dr. WALENSKY. As I mentioned, I think that these have to be locally driven, both based on vaccination as well as based on background rate of disease. So—

Mr. CLINE. But that is a pretty good softball for you. Do you have to be 100-percent vaccinated to open back up and stop wearing masks?

Dr. WALENSKY. No, I don't believe so.

Mr. CLINE. Okay. Thank you.

Let me ask you about the business community. The livelihoods of many businesses in my district have been threatened over the last year as they worked to adjust to the changing environment during COVID. As more has been discovered over the last year, guidance has changed as well. A Federal Reserve study found that the pandemic resulted in the permanent closure of roughly 200,000 U.S. businesses.

What will you do to empower States to determine how best to govern so that overly burdensome recommendations and regulations from the Federal Government do not cause further harm?

Dr. WALENSKY. We have been putting forward—first of all, we are working to get people vaccinated. Because I think, as we have seen, when people get vaccinated, disease rates in their local areas come down, and that is the ticket out of this, in my mind, when people get vaccinated.

We are working really hard with all jurisdictions, with all communities, at the State, the local level, to get people vaccinated to ensure confidence, to provide the best information possible so that people feel empowered to make these decisions, that they are the right decisions coming from trusted messengers in those communities.

And so we are working to do that at the public health level. And then we are providing the guidance that can lead to informed decisions in communities with local jurisdictions, with Governors—I spoke to the Governors yesterday—to make sure that our guidance is applied in a safe manner at the local level.

Mr. CLINE. Thank you.

I yield back.

The CHAIR. I would like to recognize Congresswoman Clark. But, for one moment, I am going to again hand the gavel to Congresswoman Lee so I can just—see, it did not work the last time, of getting to Homeland Security, and I will get there and get right back.

So, Congresswoman Clark, you are recognized.

Congresswoman Lee, take the gavel.

Ms. CLARK. Thank you so much, Chairwomen.

And thank you both for joining us. And just the deep gratitude of a Nation for the work of the CDC and the response to this pandemic.

Dr. Walensky, you and I have talked about the value of public service, the importance of treating public health jobs as we would a career at DOJ or Defense. Are there programs or incentives that the CDC would like this committee to prioritize that would address the needs of our public health workforce?

And, in particular, how can we work with the CDC and State and local level to build a more diverse public health workforce?

Dr. WALENSKY. Thank you very much, Congressman Clark.

I think one of the things that is really important here is to make sure that the compensation is competitive with the private sector in our public health jobs. As I talked to the State health officials, they would tell me they can't hire an M.D. In a State public health—the compensation wasn't competitive. Somebody who came out of medical training and medical school with, on average, \$200,000 worth of debt was not going to enter the public health workforce, because they didn't have salaries that are competitive.

As we are working on expanding our “disease detective” EIS program, one of the things we are really looking forward to is hoping to do loan repayment programs.

And across our workforce, of our training, loan repayment programs would really go a long way so that people could enter into public health, which obviously pays less than the private sector. Many of the training programs that we would put forward to be tuition-free, to be accessible to people who have had less resources.

Ms. CLARK. Great. Thank you for that.

And anything specific around your plans and strategies for increasing diversity in your workforce?

Dr. WALENSKY. We are reaching people where they are. We are working to, you know, go to historically Black universities. We are working in communities to try and bolster people within the communities.

We have the potential now, as we are scaling up our workforce within public health that we have had to do by necessity through this pandemic, to retain them. These are people who are interested in public health. They have demonstrated, they have volunteered to help. And now is the time to scale them up, to retain them, and to make sure that they can continue the important work they have been doing, to continue the outreach that they have already made, to maintain that network. And that, I think, is really going to be key for our next step forward.

Ms. CLARK. And just really quickly, if an employer made a decision around masks based on two different groups, one that had a 96-percent vaccine rate, one that had a 77-percent vaccination rate, would you think that was a fair way and aligned with the science to make a decision around masks at the workplace?

Dr. WALENSKY. Most definitely. Almost every morning, I look at a map of vaccination rates across this country by county.

Ms. CLARK. Thank you.

Dr. Schuchat, I was wondering if you could tell me a little bit about the gun violence research that was first funded in 20 years in the fiscal year 2020 budget. And I wondered if you can tell me what you are learning in our research on firearm injury and mortality prevention.

And we just so appreciate you treating this as the public health crisis that it is. And any updates and strategies and interventions that have emerged from the research that you can share?

Dr. SCHUCHAT. Thanks so much for that question, Congresswoman Clark, and for the congressional resources that we first got in 2020. Our call for proposals for firearm safety opened a flood of applications, and we were really pleased to be able fund several that were focused on the gaps that the National Academy of Medicine had identified.

The scientific research that we are supporting is helping us understand firearm-related injury across different types of incidents, different types of populations, and different settings.

We had 18 funded sites in that research. They are looking at firearm behaviors and co-occurring mental health and behavioral risks among youth. They are looking at individual- and neighborhood-level risks for firearm-related violence so that communities can de-

sign tailored interventions. And they are setting a clinical screening tool to assess youth risk for future firearm violence.

These are really important projects that span the Nation. But I can say, we had so many more applications than we were able to fund. So the ability to scale it up is going to be precious.

The other aspect of the resources that we received helped us strengthen the data gathering on the surveillance, just so we would know who was getting injured by firearms and where these events were occurring, when they were occurring, so that we could understand trends and risk factors.

So I think it is a really important, precious area for us to continue.

Ms. CLARK. Thank you so much.

I see my time has expired. I yield back, Chairwoman Lee.

Ms. LEE [presiding]. Thank you very much.

Now I will yield to Representative Frankel.

Ms. FRANKEL. Good morning. And thank you both, Doctors, for all your good work.

And not to monotonize this discussion on Members wearing masks, but, Madam Chair, I just would respectfully suggest that our colleagues who do not want to wear masks, whom we have heard from today, ask their colleagues who have not gotten vaccinated to get the vaccine.

Because, you know, I think I speak for most Americans who have been vaccinated. And we don't want to wear masks, but we do not want to be sitting in small areas with people who are refusing—who know better, who are refusing to get vaccinated.

So my next question, Doctor—either of you can answer this—is, what is expected for when we are going to need boosters for our vaccinations?

Dr. WALENSKY. Thank you for that question, Congresswoman. And congratulations on your grandbaby, who I think was pending as we last spoke.

Ms. FRANKEL. Yes, he is here, thank goodness. Something good came out of the pandemic.

Dr. WALENSKY. That is right.

On the topic of boosters, I think that it is really important for us to understand several things.

First, if you have received two doses of vaccine or you are completed vaccinated, right now you don't need a booster. You are protected. Or, at least, the data that we understand now for the general population implies that you do not need a booster right now.

I think all of us recognize that we don't want to be back to where we were again. And so we would like to study this. We are studying when we might need a booster.

And, in fact, that gets back to the, what are the true correlates of protection? We do know that antibody levels, over time, we have seen they wane. And so the question is, when they wane, are these people still protected? What do these quantitative numbers mean with regard to protection?

We also know, importantly, that we vaccinated first our most vulnerable. We vaccinated people who are in long-term-care facilities, we vaccinated our elderly, we vaccinated people who might not have had the most robust immune response to start.



And so we are looking at the timing of when boosters might be needed. Will it be 6 to 9 months, will it be 9 to 12, or 1 to 2 years? We have seen data from SARS, the SARS-1, that has demonstrated reinfections after 2 or 3 years. That is after natural infection.

And so I think the most important thing is, we certainly want to be ready. And so that is where we are right now.

Ms. FRANKEL. That is good.

And do you expect, though, that with the next shots, we are going to be able to get them like with the flu shots, you know, not having to go to mass sites and things like that?

Dr. WALENSKY. I think one of the things that is really important to recognize here is, we don't have an adult immunization structure in this country. We haven't. We have a childhood immunization structure in this country, but we do not have one for adults. We don't have a mechanism to do this right now.

And among the reasons for the funding is to develop and bolster an adult immunization structure in this country, for flu shots, for COVID vaccines if we need them again. That would be the vision for Shingrix, for all the other—for, you know, tetanus when we need tetanus updates, for all of the things. We don't have that mechanism right now.

Ms. FRANKEL. Well, thank you. That is a good idea. Because our rollout in Florida of the vaccines was chaotic. I said it was like "The Hunger Games" here. So, I mean, it was really—it was frightening.

You know, I think one part of our population that really suffered were the elderly, and I am just interested in whether you are doing any work to address, you know, how we handle these kinds of situations with our elderly population. There was so much isolation and depression.

Dr. WALENSKY. I think—you are noting the elderly specifically, and I totally agree, the isolation here had been so challenging, and in long-term-care facilities, so devastating to watch. But I think you are raising a larger issue too, which is, the mental health of this Nation has suffered.

And so we are doing a lot of work in collaboration with SAMHSA, to evaluate mental-health-related issues, to look at issues related to suicide, to do more surveillance, and to do outreach with interventions that are data-driven, that have toolkits provided by the CDC for how we can do outreach in these communities with community workers to really do evidence-based science in mental health across the age spectrum.

Ms. FRANKEL. And real quick, talking about toolkits, how about in terms of ideas for communities on how to increase vaccination rates? Is there a place that our health departments can go to get different ideas or strategies?

Dr. WALENSKY. Yeah. Thank you for that. We have an extraordinary number of resources.

We have vaccine confidence consults. You can call the CDC and get a vaccine confidence consult.

We have, through HHS, the We Can Do This campaign. It is 5,000 community corps. So if you have a group that NASCAR speaks to, you can go get your vaccine and then take a ride around

the Talladega track. So there are lots of different ways to engage with this community corps through the [wecandothis.gov](http://wecandothis.gov).

I would really encourage your State departments to engage these community corps organizations, be it NASCAR, NFL, country music, or Infectious Disease Society of America. Faith-based organizations can really help do the outreach so that people are talking to people they trust.

Ms. FRANKEL. Thank you very much.

I yield back, Madam Chair.

The CHAIR [presiding]. Let me thank my colleague, Congresswoman Lee. Mission accomplished.

And, with that, let me recognize Congresswoman Bustos.

Mrs. BUSTOS. All right. Thank you, Madam Chair.

And, Dr. Walensky, thank you so much for taking time earlier in the week to chat. I am going to talk with you a little bit as an extension to what you just shared with Congresswoman Frankel about new ways and innovative ways to reach out to people, specific, in this case, to rural America.

I talked with Dr. Fauci about this yesterday at our hearing. He was going to take the questions that I was asking about reaching rural residents and try to come up with some new ideas.

But I want to talk specifically about the disparity between those who live in rural counties compared with those who live in more urban counties. We know by the numbers that CDC has released that it is less than 40 percent of residents in rural counties who have received at least one dose, compared with just about 46 percent in urban counties.

And so I want to hear your thoughts about vaccine hesitancy, other issues that are specific to rural counties.

If I may throw out an example, in the congressional district that I serve here in northwestern Illinois, we have one county, which is a couple counties south of where I am talking to you right now, it is along the Mississippi River. The entire county has 6,700 residents. And early in the—for people to sign up for the vaccine, they just had a couple phone lines. Broadband is spotty at best. Their volunteer corps, as far as getting people out to help, were very, very senior themselves and were concerned about getting COVID themselves, so that was all brought to a halt. They were registering people. There was no online portal to register. It was all hand-writing, you know, paper and pencil.

And so, now, with the announcement that just came out earlier today, where we have half of the adult population that is vaccinated, in this county only 19 percent overall is vaccinated. And so, just these great big disparities.

So I am just wondering, Dr. Walensky, on top of what you just talked about, I am very curious, like, can I get a Chicago Bears player to come to Henderson County? I mean, I am just wondering how that might work.

But what steps is the CDC taking to increase these vaccination rates in rural areas? And, specifically, also, how we can address vaccine hesitancy. And maybe even really talk through, like, these celebrities, because maybe that would be a way to have this work. I am wondering if we could get some folks in my neck of the woods to help out.

Dr. WALENSKY. Thank you for that question and for highlighting data that we have discussed about these discrepancies in vaccine rates really through the end of April.

Another piece you didn't actually raise is the discrepancies in telehealth, right? In rural counties, it would be so helpful to have telehealth. And yet we saw in a previous MMWR that telehealth wasn't reaching, for exactly the comments you said—broadband, telephone, you know, decreased access.

I think it speaks to the fact that we don't have community workers in these communities that have had a long-term public health infrastructure in these communities to do the work of public health. We don't have a public health department that is sustained, that has been viable, that has been well tended to, that has competitive salaries, respected positions, and community workers in those communities to do the work that you are talking about.

And that is exactly what—we have had resources that have gone out that are specifically line-itemed for rural areas because we recognized that deficit through the context of COVID. We have had community-based organizations specifically outlined for rural areas through the context of COVID. And what we are asking for, not just to have it for the context of COVID, but now you are going to find them, you are going to find these people who are devoted to this community work.

We need to make sure that they are trained. We need to scale them up. They need to be able to interact with the data systems. You don't have data systems there for people. You are doing it by hand, by paper and pencil. That is not a way to do public health in this country in 2021, never mind for what we need to reach for in 2030.

In terms of what we are doing now, you and I discussed, you know, I was in rural Georgia, and it was really incredible to talk to the people who are doing this work, who are going door to door, the elderly people, as you note, and who are hearing, "The National Guard didn't work." What did we need to do? We needed to be at the change of shift at 4:00 a.m. And have people trip over us and say, "Can you get your vaccine now?" That is the kind of grassroots efforts that we are moving forward with now.

We have these confidence consults, that people can call the community corps. I am a Patriots fan, I am sorry to say, but I bet the Bears might be something to facilitate. You know, I do think when you call these—wecandothis.gov, you will get a wealth of resources. These people want to help.

Mrs. BUSTOS. Good to know.

Dr. Walensky, again, thank you to you and your team for all you are doing to help our country get past this pandemic. Grateful to you.

With that, Madam Chair, I yield back.

Ms. CLARK. I don't think you need to apologize for being a Patriots fan, though.

The CHAIR. Now we get to the real core of the issues here. But my hope is that you are a Yankees fan so there doesn't have to be a Red Sox fan here.

Right, Katherine? Anyway.

Congressman Harder.

Mr. HARDER. I don't know if I want to get myself in the middle of this. But thank you so much, Chair DeLauro, for hosting this hearing.

And thank you so much to the witnesses for taking their time. And a special thanks to Dr. Schuchat for your decades of service.

One of the things that I really wanted to focus on is how this pandemic has highlighted some of the gaps in our public health system. And I think one of things that has become abundantly clear to me is just how critical a strong, well-funded public health workforce is to care for folks across the country, especially in rural districts like mine, where capacity, especially healthcare capacity, is already thin.

I have seen the beginning of some grant announcements out of the CDC that are going to help fund some of the programs outlined in the American Rescue Plan, specifically the \$7,000,000 investment to hire and train public health workers.

Dr. Walensky, could you describe the rollout of the public health hiring and training programs and especially how the CDC will support these positions on an ongoing basis after the rescue funds expire?

Dr. WALENSKY. Thank you for that, Congressman.

You know, we just put out the first tranche of \$7,400,000,000. Really, \$4,400,000,000 is intended to help scale up where we are now to get us out of this pandemic, to do the hard work of continuing testing, continuing disease diagnostics, continuing workforce for lab and genomic surveillance, and to make sure that we are—and vaccine distribution and community workers for that vaccine distribution.

The other piece of it, the \$3,000,000,000, is an investment in the future, to be able to take that infrastructure and to invest in the workforce that will be moving forward.

But I think the most important thing you highlight is that these are not one-time investments. One-time investments will not fix the problem that led to this pandemic of COVID-19 and our inability to handle it. They need to be sustainable. They need to be long-standing. They need to be keeping the pace with inflation. They need to be keeping the pace with technological advancements. And so this is an investment now, but it needs to be a sustained investment over time.

Mr. HARDER. How will it be a sustained investment over time? Do you expect that to be—I haven't necessarily seen that investment in the budget document. How do you expect that to manifest itself in the discussions we are having today?

Dr. WALENSKY. I think this is going to be a continued conversation. I think I am going to probably see you here this time next year to demonstrate all the hard work that we have been able to do with the resources that we have had and what we still need to do in the years ahead.

Mr. HARDER. Well, I look forward to working with you on that and especially, I think, making sure that rural areas that are especially strained in some of the public health capacity, like our district in the California Central Valley, have some of the opportunities to get some of these grants, because I think it is very much needed.

My second question is, you know, just a little bit more broad, and to you, Dr. Schuchat. I think we have a tendency to only invest in public health during times of crisis, and I think we need to be doing a lot more to improve the capacity of State and local public health departments, not even for the pandemic we are dealing with now but to prevent others in the future.

What else can we be doing to consistently and sustainably equip public health departments for future public health emergencies and especially for the special considerations we may need for rural districts?

Dr. SCHUCHAT. Yeah. Every aspect of an emergency response is improved by the work that is done beforehand, the relationships that have been built, the data systems that are in place, the skill level of the staff, and the familiarity that they have with the communities and the other organizations nearby.

We were not ready for this pandemic. Our data systems were very far behind, and our public health workforce was gone, basically, you know, the 60,000-some jobs that were no longer filled. And so, you know, looking back on what has happened over the past year and over the past few decades, I think we can see that we just need to do better going forward.

I want to say a few words about the public health data modernization, because I think that left us lead-footed at the beginning of this response, with not really knowing what was going on and not being able to keep up.

And so we know—you know, I have talked to healthcare executives who have described investments in a single hospital of \$700,000,000 versus, you know, what our initial resources were, \$50,000,000 for the entire public health data modernization effort.

I think, going forward, we really need to take data and its complexity and the full ecosystem seriously, both with data scientists and with interoperable systems, migrating our systems to the cloud, strengthening what public health local and State capacity is and also what the CDC's is.

So that is a really big, complex job. And it also relates to what Dr. Walensky was describing, where it is tough for public health at any level to be competitive with the private sector. And so we have to figure out how to attract quality individuals to work with us and have strong public-private partnerships to go even further.

So I see data hand-in-hand with workforce in getting us out of the state of preparedness that we were in.

Mr. HARDER. Excellent. Yeah, you can't fight what you can't find. Well, thank you so much.

And, with that, I yield back, Chair DeLauro.

The CHAIR. Congresswoman Watson Coleman.

Mrs. WATSON COLEMAN. Thank you, Madam Chair.

Dr. Walensky, thank you for all the work that the CDC has been doing, not only in this space as it relates to getting us through COVID and having an after-COVID experience, but all the other work that you all do at the same time.

And, Dr. Schuchat, thank you so much for your 30-some years. God bless you. You have been enormously important to all of us and our well-being, and we wish you the very best.

Dr. Walensky, I am sorry that we didn't get a chance to talk beforehand, because I have, really, a lot of questions. I am just going to raise some of them, but hopefully we will talk about them a little bit further down the road.

I want to talk about the gun violence issue. I appreciate the fact that we funded research for the first time in, I guess, a very, very long time, and that is being used valuably by you all.

I am wondering, with the President's new initiative where he is talking about more local interventions, what that means. How do you see that rolling out? What are the kind of interventions that will have an impact on the kind of violence and death by guns that we see in our communities now, particularly our inner-city and low-income communities?

Dr. WALENSKY. Thank you so much for that question, Congresswoman.

We are really looking forward to seeing how the investment of the initial funds from fiscal year 2020 and 2021, and as those data mature, what we learn, and then really looking forward, using the template of the information that we need from the National Academy of Medicine to inform the kinds of research that is being done.

Of course, that research, as you note, has to be at the local level. It has to be related to behavioral health and mental health, but, importantly, it has to be at the neighborhood level and at the level—and because, you know, not every neighborhood is going to be the same.

So the science that we are going to do is going to be about the who, the how, the why of firearm injury prevention. And we are going to move forward, and I really look forward to seeing how that science matures.

Mrs. WATSON COLEMAN. So do you think we are at the beginning of that? And how long will we see the actual implementation of effort evidenced by the research that was being done? Because we are in a very urgent, crisis situation with gun violence in our communities.

Dr. WALENSKY. I would agree with you. I will say, we will need to, sort of, see what the science demonstrates, and then we are going to implement at an actionable level within those communities. We need to understand what the science says before we can act. And we are really looking forward to seeing how that evolves.

And maybe Dr. Schuchat?

Dr. SCHUCHAT. Yeah. Just to expand a little bit, you know, we had that first investment of the \$3,000,000 in this work, but the proposed expansion—excuse me—the proposed community violence work is a larger scale.

And the idea there is to take what we have shown to work through the technical packages that we have issued on violence, including on youth violence for instance, and to scale those up, to have communities take on the ability to implement proven methods.

They may involve, you know, strengthening connectedness between kids and schools and adult mentors in the community. It will really vary community to community. But we are hoping to fund a large number of communities to really take those to scale.

Mrs. WATSON COLEMAN. And, Dr. Schuchat, I am really interested in hearing some of the specifics that are going to be employed under this effort.

The President also said in his skinny budget he wanted to end the HIV/AIDS crisis. And one of those things I think is very important in this is the bill that I sponsored with regard to PrEP.

And so what I am wondering is—two things. Number one is, what do you say about the trend in HIV/AIDS right now? Is it still going down? Do we see an upshot because of the pandemic or whatever?

And what do you think of how the resources should be applied? How are we going to ensure that they are applied across the board to all races and communities?

Dr. WALENSKY. Thank you for that question. As you know, prior to my coming here, my career was in HIV disease and prevention. I am an HIV doc by training.

Yes, I think, you know, right now, the Ending the HIV Epidemic initiative has been invested in 57 jurisdictions with the highest rates of HIV. I think that, as with many diseases that were pre-occurring before this pandemic, they have been exacerbated by social isolation, by inaccess to medical care, by many things. We are looking at the investments that were made in those 57 jurisdictions, some of the lessons learned there.

As I am certain you are aware, with your interest in pre-exposure prophylaxis, it is not getting to the communities that need it, necessarily, for cost reasons, for access reasons, behavioral health reasons, that places that have the highest rates of HIV actually have the lowest rates of pre-exposure prophylaxis use. And that mismatch is something we need to fix in the years ahead.

Mrs. WATSON COLEMAN. Thank you.

I know my time is up, but I think that that is a crisis that needs to be addressed. That is what we saw with testing for COVID. That is what we saw with contact tracing. That is what we are seeing in some respects with vaccinations but not as much. And so that is a crisis, in and of itself, as it relates to poor communities or minority communities. And I want to know specifically at some point how we are going to get at those communities.

I thank you, Madam Chair. I yield back.

Thank you, Doctor.

The CHAIR. Thank you.

Congresswoman Lawrence.

Mrs. LAWRENCE. Thank you. Good morning.

As you know, I represent Michigan and was very involved with the lead crisis in Flint. And we know that lead exposure is unfortunately prevalent across Michigan, and that includes the lasting effects of the Flint water crisis. I am proud to work with my colleague, Congressman Kildee, to provide funding for the Flint Lead Exposure Registry at the CDC.

Dr. Walensky, I am incredibly concerned with the high levels of lead in cities across the country, especially in the schools. When I talk to my colleagues, there are numerous schools that put the plastic bag over the drinking fountain, with no research of how long the children drank from that water fountain before we put that plastic bag over it, the lasting effect.

Can you speak to how the CDC will utilize the Childhood Lead Poisoning Prevention Program with more targeted initiatives like the Flint Registry to combat lead poisoning in our communities, especially the impact it has on children and their developing brains?

Dr. WALENSKY. Thank you very much, Congresswoman.

And one thing I think we learned from this pandemic—and this was reported in the MMWR as well—is the decrease in lead poisoning surveillance that happened because of the pandemic or lack of access to care.

I think one of the things that we will really understand as we invest in our public health infrastructure is different communities need different things. We heard in rural communities they need broadband, but in other communities we need investments in our community workers to do surveillance of lead.

We are doing active surveillance, and maybe I will ask Dr. Schuchat to chime in as well.

Dr. SCHUCHAT. Just to thank you for your leadership around the Flint crisis. And, you know, the registry has been incredibly valuable for the community as a community-owned and -led response. You know, the children affected potentially could have long-term consequences, but with mobilizing wraparound services and engagement, we hope that some of that will be mitigated.

We don't know how many other communities are in the same boat that Flint was in, and that is part of the focus of expanding lead surveillance through the public health systems. There are other departments that are really engaged in investments that can help reduce the exposures, the lead pipes and so forth that you mentioned, but we think that data is the first thing. We have to know what is going on to be able to target effective responses.

And, ideally, those are community-owned, the way that they were in Flint, to not just have, you know, a distant government trying to figure out what was going on but having those community workers who could help the families that are affected.

So I share your sorrow about what happened and enthusiasm about the registries and the ability for us to strengthen surveillance around the country.

Mrs. LAWRENCE. I will tell you, if we had a hearing on lead poisoning, many members will step up and talk about the concern they have in our communities, urban and rural.

The last thing I wanted to add is to add my voice to gun violence. We know for decades there was a refusal to establish or identify gun violence as a health crisis, because, for whatever reason, administrations did not have the wherewithal or the desire to do the data, as you talked about, so that—we knew that we could use the data from car crashes to implement safety belts and airbags, but we have never had the courage to see through the research so that we can begin a federally led program to address gun violence.

And I just want to tell you why this is so critical. In 2020, there were 327 homicides, 1,017 nonfatal shootings in Detroit alone, a 19- and 53-percent increase respectively. This problem is not getting less; it is increasing.

And this obsession we have in America with guns, I can only see it getting worse. And for mayors—I am not a mayor, but for people



in Congress who are seeing these deaths so frequently, this has to be a priority.

So, with that, I want to yield back and say thank you so much for everything that you and the administration are doing.

The CHAIR. Thank you so much.

And we are now going to move to round two, and I think we have the time to do a 5-minute round. So thank you very much.

I want to begin by, I know several of my colleagues have addressed the firearm injury, the mortality research. And I just wanted to say that I was so proud that this subcommittee held the first hearing in 20 years on gun violence prevention research. And we began funding for the NIH and for CDC, the ability to do this research, which can take a look at suicide, can take a look at gun storage, and a whole variety of other areas that could help bring relief to prevent this violence.

And I am pleased that the President's budget proposes to double the funding to \$25,000,000. My hope is that—but I just have a very quick question here, because I want to get to a couple of others.

And I guess, Dr. Schuchat, when do you believe that you will have the opportunity, or CDC will have the opportunity, to share some results?

Dr. SCHUCHAT. Yeah, the research projects are in progress, and, you know, I hope that within a year or 2 there will be preliminary results from the initial investments. You know, they are doing extraordinary work, but, as you know, research can take time, and these are complex issues to fully investigate.

The CHAIR. Right. Thank you. Thank you very, very much.

Let me ask both Dr. Walensky and Dr. Schuchat, this is about cardiovascular disease in women. Heart disease, stroke continues to be a leading cause of death of women in the U.S. In 2017, nearly 300,000 women died as a result of heart disease.

And the research shows that women often experience different symptoms of heart attack than men, leads doctors to misdiagnose women, results in worse treatment outcomes. Critical for the CDC to support an education and an awareness campaign in all 50 States and territories on heart disease so that women can receive appropriate care.

My question is to both of you. Give us an update on CDC-supported activities to educate women about heart disease and cardiovascular health, and the need to create an urgency about our looking at this issue to impact the research that needs to get done.

Dr. WALENSKY. I am going to let Dr. Schuchat start with that one. Thank you.

The CHAIR. Okay. Thank you.

Dr. SCHUCHAT. Sure. Thanks so much for raising this issue. It is so important as a leading cause of death in women and as an underrecognized, preventable problem.

We know women are less likely to—they have atypical symptoms. You know, I was telling colleagues the story about my mom, you know, had neck pain playing tennis, which we thought was arthritic, and it turned out it was angina, and, you know, fortunately got surgery in time.

But it is very common for women to have different symptoms, delay, to be detected later because of clinician as well as bias and

to have bad outcomes because of that. So I think there can be benefit from education and communication efforts.

You are familiar with our Million Hearts initiative, which is really trying to get hypertension to be well-treated, to prevent a million heart disease and stroke events, which takes public and clinician and institutional effort. And I think that the communication and education call that you raised can be done as part of that system.

We are working together with the Center for Medicare and Medicaid Services in partnership on this, and education and communication campaigns are part of that.

Obviously, you know the Wear Red event that I have seen many Congresswomen be part of, that can't just be a 1-day or a 1-month thing. It needs to be year-round and sustained, because there are a lot of preventable deaths that we could attend to.

The CHAIR. Uh-huh. Thank you. That is going to be one of the issues I would like to focus on, you know, as we move forward.

I just wanted to ask this question, and this is about the global response to COVID. We have made significant progress here, but the pandemic will not be over until there is a global success.

Dr. Walensky, how is CDC working with international partners to support the global response to COVID? How is the agency planning to expand surveillance, prevention, and response to pandemic threats around the globe?

Dr. WALENSKY. Thank you very much.

A threat anywhere is a threat everywhere, right? And so we do, we have a responsibility to not just take care of ourselves but around the world. CDC has collaborations in 60 countries, 150 sites, and the ability to have these collaborations that have been longstanding have served us well.

So, for example, we have a regional office in India that is 20 years old. We have trusted colleagues there. They trust us. For the last year, we have been training up infection control preventionists in India, over 10,000, within these collaborations within country. So, when it came time and India was having challenges, we were able to mobilize those collaborations. We were able to rapidly get oxygen canisters to India.

Our work at CDC is really in our technical surveillance, our technical advice, our technical and scaling-up capacity. And it really is critical to have those trusted people on the ground so that we are able, in times of crisis, like we also have done in the Congo and Guinea for Ebola just this past year as well, to be able to scale up in times of crisis. And so that is exactly what we are doing and what we are looking for resources to be able to continue.

The CHAIR. Okay.

I know my time is up, but I want to make this one comment. I was pleased that the administration and Ambassador Tai was at the WHO and talking about lifting the waiver on supplying India, South Africa, other countries with the opportunity for the benefit, in a temporary way, of the licensing, the patents, et cetera, so that they can deal with manufacturing.

Your point earlier, it is not good enough for us to be 80, 90 percent covered and 20 to 30 percent in other countries, because we are at risk if that is the case. So I look forward to working with you on that effort.

Congressman Harris.

Mr. HARRIS. Thank you very much, Madam Chair.

And, again, thank you, Doctors, for coming before the subcommittee.

And I would be remiss—I forgot to thank Dr. Redfield, a fellow Marylander, for the work he did at CDC. You know, the job sometimes—you have to take slings and arrows, no question about it. Because, if you recall, he was highly criticized for suggesting that the Wuhan virus came from a lab in the Institute of Virology, castigated in the public media. And now it seems we have come 180 degrees around where that is actually something that we actually should look at if we are to truly determine how this got started and where it came from.

But let me go ahead and just ask about—and just to clear something up, by the way, the—because it was suggested that somehow Florida had kind of a bad response to COVID, I guess. I don't know. I think that Florida actually has among the lower rates of infection. And despite the possible description of a vaccine rollout as hectic, it seems that the public health goal should be to get to a good result, and I think Governor DeSantis did. That is just my comment. I mean—and it is objectively backed up by objective data, which is what we should be talking about, is objective data.

So let me just ask a brief followup on gun violence, because, last year, in the 28 largest cities, there was a 36-percent increase in gun violence between June and October. Very briefly, any ideas, what could possibly have resulted in such a huge increase in gun violence in our cities?

Dr. WALENSKY. Thank you, Congressman. I also—or Dr. Harris. I also neglected in our first round to applaud you and thank you for all of your public service in trying to get people vaccinated. I did want to highlight that and thank you for that.

We are actively doing research on firearm injury prevention, as highlighted by the priorities of the National Academy of Medicine, the who, what, when, and how of gun violence, of firearm injury. And we will look forward to those studies.

Mr. HARRIS. Okay. No, thank you very much, because I think we have to get to the root of the increasing gun violence and then question whether or not it is because policing activities have decreased. Many police forces in my local jurisdiction, for instance, have up to a third of their positions vacant because you can't find someone who wants to be a law enforcement officer anymore.

The other thing that I wanted to ask about is the data. As you look at robust data collection, I would hope two things. One is that you do it, obviously, across the various parts of the CDC and bring it into what you suggest, Doctor, should be the way we collect data in 2021, not on the backs of envelopes, and develop a robust system, because it certainly is necessary.

But as part of that, I do hope that you look at what went on with nursing home deaths in New York during the COVID epidemic. Because I think we owe it to our seniors to understand what appears to have been data manipulation in New York, and I think we need to get to the end of it.

Now, I will just close out the last minute and a half and ask you to update us on Zika, which we haven't heard about for a while,

thank goodness. Zika and—very briefly, you in passing mentioned Ebola, but we know that it is still simmering in Africa. What are the threats of these two diseases right now to Americans?

Dr. WALENSKY. I am going to pass that to Dr. Schuchat, but just sort of comment and say that, among the things that I think of as critically important is the investment in SET-NET, which is the review of mother-baby pairs, which I think helps us evaluate not only Zika but also COVID-19.

But Dr. Schuchat?

Dr. SCHUCHAT. Yeah. I think there are a lot of lessons from the Zika epidemic, you know, a virus that had been recognized many years earlier with a mild syndrome, but a lab test that was developed because of that initial outbreak in Yap, and then, you know, the introduction into our hemisphere and the terrible outbreak in Brazil and then in many other countries, including southern U.S.

That reminded us how important it is to have entomologists in public health, a discipline that had been lost, and to have surveillance at the local level for mosquitoes. We know there are a lot of threats right now in mosquitoes and ticks and other vectors that can be the carriers of new diseases to susceptible populations.

So the result of the Zika work was strengthening that infrastructure that we have with some centers of excellence, the SET-NET that you just heard about that helps us track not just Zika but other threats like opioid-related harms, syphilis, other things that can affect mothers or babies.

And so it really gets back to the public health infrastructure and the need for sustained focus. We get investments, and then we lose them, and then we are surprised when a new threat takes us without preparation.

I can tell you from meetings with the World Health Organization, they were very concerned about loss of researchers to be able to continue to understand Zika as it hit newer communities that hadn't yet been through what we went through in the Americas.

So I just think the emerging threats are out there and that we need systems that are agnostic to pathogen or agnostic to disease that protect all of us.

Mr. HARRIS. Thank you very much.

I yield back.

The CHAIR. Congresswoman Lee.

Ms. LEE. Thanks very much.

For Dr. Schuchat: One lesson that we learned during COVID-19 was the need for consistent, standardized, disaggregated, culturally appropriate data collection methods to really determine how to address and where to address targeted resources for medically underserved communities.

Now, this was a heavy lift. We put this in all of our legislation. We asked CDC to collect the data, to work with States, to give us the information as it relates to language, and to disaggregate the database on race, ethnicity, gender, socioeconomic status. We never really—I don't think CDC ever took us seriously.

So I am wondering now, where are we in terms of data collection? Because we have to know, not only for COVID, but also for any healthcare initiatives that disproportionately impact people of color.

And then, Dr. Walensky, let me follow up. I wanted to just ask you, following up from Congresswoman Bonnie Watson Coleman's question on HIV and AIDS, you know, we have an HIV/AIDS national strategy and plan. We went around the country seeking input from impacted communities to develop this plan.

And I am wondering if we have an update of a national HIV/AIDS strategy/plan and if we have a point person in the White House who is really putting all of this together and coordinating it.

Dr. Schuchat.

Dr. SCHUCHAT. Yeah, thank you. I really appreciate the attention that Congress gave to race and ethnicity and socioeconomic variables. And it was a tragedy at the beginning of the epidemic, how behind we were.

We are not done with improvements, but this has been a very high priority for the administration and the CDC, and we have made it a priority for State and local public health.

They are somewhat hamstrung by what data they have access to, and so we have been trying to take a systematic approach to address both tracking cases, hospitalizations, deaths, as well as vaccinations, in a way that gives us complete, actionable information.

We have been using something called the Social Vulnerability Index, which has really driven where we try to get vaccine access to be improved. And that has borne results. We have seen narrowing of the disparities of who is getting vaccinated.

We have deployed through partners, with HRSA and FEMA, to get federally qualified health centers out in the areas of greatest need, to get the pop-up and the mobile clinics that FEMA is facilitating into the areas of need.

In our pharmacy partnership, we have been reaching much greater percentages of individuals who reside in high Social Vulnerability Index areas. We have been looking at the ZIP Code level, not just the county level, to get those resources out.

And I just really applaud Congress for saying this is important, you have to do it, and us being able to have the resources to try to follow up. But it—

Ms. LEE. Thank you. And I would like—we only have a couple minutes left—to get a report back from CDC at some point on the status of what we asked for in all of the legislation, as it relates to data collection, if that is possible.

Dr. SCHUCHAT. Yes. And we have been providing a monthly update on the data systems, but I think a more comprehensive one, I am sure we are happy to follow up on.

Ms. LEE. Thanks a million.

Dr. Walensky, what about—and like you mentioned earlier, we have known each other for many, many years, as it relates to getting a handle on how we achieve an AIDS-free generation by 2030.

So have we updated our national AIDS strategy? And are we coordinated now with the White House in implementing one, if we have one?

Dr. WALENSKY. I—well—so what I know is, I used to use that AIDS strategy as my research bible. These are where we needed to study, so I am very familiar with it.

I am not familiar—I don't believe we have yet updated it in this administration. Of course, this administration for the last 4 months has been really focused on making sure that we can get out of COVID so that we can focus on other areas of health.

But I do know that, in the months ahead, when COVID is no longer what we are doing most of the time, that this is a high priority for this administration. I will look forward to that.

Ms. LEE. Okay. Thank you.

Madam Chair, I will yield the balance of my time. And thank you again, Madam Chair. Thank you.

The CHAIR. Thank you.

Congresswoman Herrera Beutler.

Ms. HERRERA BEUTLER. Thank you, Madam Chair.

I wanted to go back to maternal mortality. I know that was discussed a little bit earlier.

In my district, two of my counties, Skamania and Pacific County, are considered maternity care deserts. And Lewis County, which is near there, is classified as having low access to maternity care. And lack of access to care stops women from receiving care that they need, especially those struggling with mental health and substance use, which I have seen a spike in in those counties and in that area.

So a 2020 or 2018 report found that the rate of maternal mortality in the U.S. could be even higher if we consider suicide and accidental overdose. And, as you know, our rates are not good.

I wanted to ask how the CDC is going to work to help the State MMRCs, our maternal mortality review committees, build their capacity to collect data on mental health and substance use issues. Obviously, they are investigating the deaths, but I want to make sure that we are collecting more and complete data to better understand that piece of substance use in mental health problems.

Dr. WALENSKY. Thank you for that question.

The high rates of maternal mortality in this country, to me, are inexcusable. This is something that we have to address.

I think you commented on the MMRCs. Not only are we interested in focusing on expanding the depth of what they do, including mental health, but also the breadth, because they are not covering every area, as you note. And so we are interested in resources to do both, expand the breadth and expand the depth in mental health as well.

I know you are aware of the Hear Her campaign, the campaign to make sure that people know and understand and can see the warning signs in the pregnancy period, in the peripartum period, and the postpartum period. And those are all parts of the efforts that we intend moving forward.

Ms. HERRERA BEUTLER. Awesome.

I am going to switch gears to kidney transplant patients and probably others who are in a similar, you know, solid-organ transplant group who are immunosuppressed.

You know, most of these folks have spent the last year in deep isolation to protect themselves from COVID, and the immunosuppressant drugs that maintain their transplant is making them uniquely vulnerable to severe COVID infection.

And now, as the vaccine becomes widely available, it has been reported that patients on these immunosuppressants obviously may not be creating the antibodies anticipated after receiving the vaccine.

What is the CDC planning to do for these communities who are following all the guidelines, getting vaccinated, but still may not be protected?

Dr. WALENSKY. Thank you. I cared for these patients last year, so I am deeply aware of, following these patients, their worse COVID outcomes and now the challenges associated with how we care for them moving forward, given the vaccine may not be protective.

We know this is true of a lot of vaccine-preventable diseases, both in the oncology world before transplant as well as in the transplant world as well. And there is a whole discipline of transplant infectious diseases for exactly this reason.

And, in fact, what you are raising is not unique to kidney transplant. This was studied out of Hopkins; Dr. Dorry Segev demonstrated it is many different kinds of transplants. And it is not just unique to transplant. They also demonstrated that dialysis patients, even before they were transplanted, didn't have as robust an immune response.

We continue to learn an extraordinary amount about these vaccines, who they protect, how long it lasts, and what we can do about it.

We have very much indicated that we will continue to need—that those patients, in order to remain protected, will continue to need to mask until we understand this further for their own health.

Ms. HERRERA BEUTLER. I think when it comes to the masking piece—you know, one of my family members is immune-compromised, and I also have small children. So I understand that tension between public and the need for my younger kids to have that access to social/emotional development, but also want to protect, you know, one of my other kids, who, obviously, a vaccine isn't going to do it. So I understand this.

I think the data really has to lead us. And that is a really easy thing to say, considering I recognize there were challenges with the last administration and politics. There are challenges with this administration and politics. That is the name of the game. But making sure that you, as the Director, the CDC Director, that it is all backed up with policies based on the data, I think is going to give us the best path forward.

No one knows all the answers on this. I don't think anybody is expecting you to do that. But the trust, to me, is the most important thing, is making sure I know I can trust the data and the recommendations that are coming out and I can back those up at home with my constituents as well. So thank you for that.

Dr. WALENSKY. And maybe what I will just add is, for those who can't get vaccinated or for those who are not going to have a robust immune response, the best protection we as a society can give them is to have everybody else around them vaccinated.

Ms. HERRERA BEUTLER. That is true. I had my shot.

Thank you.

The CHAIR. Thank you.

Congresswoman Clark.

Ms. CLARK. Thank you.

And staying on children and the pandemic for a moment, we know that kids are at a lower risk for severe infection, but my understanding is that COVID-19 has also become one of their top 10 causes of death in this country, which is, of course, a cause for alarm.

What do you see as the benefits of vaccinating our children and youth? And when do you expect to have enough safety data available to vaccinate a child of any age?

Dr. WALENSKY. Thank you for that question, because I do think that some of the data and numbers are hard. You know, it is the case that a young person may be less likely to die of COVID-19 than an old person. But a young person is less likely to die of anything than an old person. And so comparing these are not always easily compared.

And when you say, like, it is one of the top 10 causes of death among young people, that, I think, really does highlight the importance of protecting our children.

And so, you know, of course I want to see what the clinical trials demonstrate and what the data shows on the safety, as they do these scaled-down trials, down from age 12 to age 9, to age 6, to age a year. As we look at those and we see the trial data that demonstrate they are both safe and effective, I think there is an extraordinary role for vaccinating our children to protect their own health, to protect their family's health, and to protect their community's health.

Ms. CLARK. Do you have any sense of a timeline, or is that just too hard to really know at this point?

Dr. WALENSKY. My understanding is they are looking for a timeline of late fall, early 2022, is the last that I have heard. I don't know whether that will be the entire spectrum or whether that will be, like, down to age 9 or age 6.

Some of this really—I hate to say it—it depends. You get outcomes in these trials when people, you know, in the placebo arm get infected. If there is less disease out there, you have less infections in the placebo arm. So, really, it does depend on where we are with the pandemic too.

Ms. CLARK. Okay.

I also wanted to talk to you about, recently, the World Health Organization urged that wealthy countries, like the U.S., postpone vaccinations for children in order to donate more doses to COVAX, the vaccine sharing initiative.

Is your agency concerned that vaccinating our children will detract from participating in being a partner and ending the global pandemic? And, sort of, how are you approaching this balancing act?

Dr. WALENSKY. I think we have to do both.

I think we were the country with the largest number of deaths across the world due to COVID-19. This was a “put on your own face mask so that you are able to help others,” and that is what we are working to do right now.



We are actively scaling up in our efforts not only to provide funds to COVAX but also to provide vaccine, as I mentioned, the 80,000,000 doses.

We at CDC are now working as those doses get donated and implemented with countries so that we can help them in immunization programs, help them with vaccine confidence, help them with adverse outcome events, surveillance, and to do all the work that we have been doing here in this country scaled up around the world.

Ms. CLARK. Great. Thank you.

And in my brief minute left, I want to go back to talking about data collection. And we know extensive evidence showing communities of color are disproportionately impacted.

Dr. Schuchat, I wonder if you can tell me how CDC's data collection has changed, and how are you working to make sure that we are collecting impact data on communities of color and disaggregating that data?

I am sorry. There is, like, no time left, basically.

Dr. SCHUCHAT. That is all right. This is such an important issue. If we don't know where the problems are, we can't address them. And so the public health data modernization effort needs to reach every community with trust and with skilled systems—you know, skilled people working on skilled systems.

We have made progress this past year with increased completeness of race/ethnicity data. We have much more timely mortality data now. The laboratory reporting has gotten to be quite speedy, but it is usually missing all the information we are interested in. So some of our highest-yield focus areas now relate to electronic health records and other data systems that can be linked to the public health information so that we can have complete, actionable, timely data.

So a lot of progress, but a lot more to do. And we do think this really needs to go beyond COVID, because the next thing is not going to be COVID. We are not done with this, but we can't develop a beautiful, perfect, pristine system for one disease and then have everything else fall behind.

You will recall with the EVALI lung injury problem, just a couple thousand cases really exhausted our data capacity. Now with many millions of cases of COVID, we have learned that we have to scale, we have to have the systems and the workforce that can handle them.

Ms. CLARK. Thank you.

My time has expired. I just want to thank you again, Dr. Schuchat, for your remarkable service. We are very grateful.

Thank you, Madam Chairwoman.

The CHAIR. Thank you.

Congressman Cline.

Mr. CLINE. Thank you, Madam Chair.

I understand the need to ensure that we vaccinate as many as possible. And, in considering that, we also want to make sure that our children are kept safe. But I am concerned that, in the effort to keep children safe, by going beyond vaccinations, to continuing to keep lockdowns in place, continuing to keep mask requirements in place—my colleague from Washington spoke to it earlier—we

are doing just as much harm as we are potentially doing good to these children.

One thing we do need to remember is that, when we are talking about COVID deaths, of the 500,000 deaths in the United States involving COVID-19 as officially reported by CDC, 238 have been in children 17 and younger. That equals 0.04 percent of all COVID-19 deaths reported in the United States.

So we do have to make sure that, as we consider protecting our children, we also consider the effects of locking down too much, keeping them out of harm's way in excess.

And, to that end, I would ask, do you have statistics on the suicide rates of children over the past year and how much that has risen?

Dr. WALENSKY. Thank you for that question. I don't have them off the top of my head.

My understanding is that there have been increase in mental health challenges with children, increase in emergency department visits. It is not yet clear, and the research will show in the months and years ahead, whether and how much those are related to lockdowns or other adverse childhood events that are associated with this pandemic, such as food insecurity and parents losing jobs and whatnot.

One thing I do want to highlight—and I want to just make sure you understand we are aligned—is, I very much believe that all schools should be open in person, full-time, 5 days a week, come the fall.

And we have put extraordinary resources and measures and outreach to make sure that that can be the case, through teacher vaccination through the month of March, which was able to vaccinate over 80 percent of teachers, and through testing initiatives in places that cannot vaccinate younger children. We have routine screening testing in the schools—extraordinary resources and efforts that are science-driven, so that we can make sure that our schools are not only open full-time in the fall but are safe to do so.

Mr. CLINE. Okay.

I want to shift over to the study that you all are going to be undertaking into gun ownership. The last study you all undertook was in 2013, I believe.

I am concerned about some bias within your organization regarding gun ownership. So I want to confirm right from the start that underpinning this study will be a recognition of the right to bear arms as a basic human right established in our Constitution and affirmed in *D.C. v. Heller*.

Dr. WALENSKY. Congressman, I don't know the specifics of that study. That is not one that I am familiar with. I am certainly happy to have our staff get back in touch with you to discuss the details.

Mr. CLINE. Okay. Well, can you commit to me that that will be an underpinning in the study that your organization undertakes as a result?

Dr. WALENSKY. You know, I would like to understand and know the study before I speak to it.

Mr. CLINE. Well, you all were just appropriated funds to study gun safety.

Dr. SCHUCHAT. Yeah, maybe I can clarify.

In 2020, we received funds to be able to reinitiate proposals for research on firearm safety, gun violence, et cetera, and have the—

Mr. CLINE. And when was the last one?

Dr. SCHUCHAT. Yeah, you are right that this was suspended since the 1990s, I believe.

Mr. CLINE. 2013 was the last one that came out, I believe. The Obama administration issued an executive order to conduct a study regarding—

Dr. SCHUCHAT. Yeah, that I am not—I am not familiar with the details.

But what I can say is that we do not do advocacy. We are funding evidence-based research. And the funds for research that we have put out have followed the research gaps that were identified by the National Academy of Medicine. So that is—

Mr. CLINE. Okay.

Well, in my closing seconds, let me just urge you to speak to the benefits, in addition to any risks associated with gun ownership, that law-abiding gun ownership provides to society as a whole by the defensive use of guns by crime victims as a common occurrence.

Although exact numbers do remain disputed, defensive gun usage by victims are at least as common as offensive uses by criminals. Estimates range from about 500,000 to more than 3,000,000 per year, in the context of about 300,000 violent crimes involving firearms back in 2008.

So there is a way to look at this issue from a balanced perspective, and I would urge you to do so.

Thank you. I yield back.

The CHAIR. Thank you.

And if I may comment to my colleague, because it has been on my watch in which we have really held the first hearing—and please understand this—it is gun violence prevention research. And it is about the public health crisis. And the amount of research has been—there has been no research in the same way that we have dealt with automobile accidents and crashes, et cetera, and what that did in terms of helping to prevent the loss of life.

And this is research that is—I guess it was our colleague, Congresswoman Lawrence, who talked about a public health crisis in this area. And that is what the research is focused on.

I will give you—and we had an entire hearing, and I am happy to provide you with the transcript of that hearing, but we are not looking into—or the dollars appropriated were not looking at gun ownership. The issue is, how do we—there are more suicides than homicides. Why do we have suicides? And those suicides are of the highest number with our veterans. Why is that happening? If we can store guns, as people across the board from wherever position are, in a better, safer way, would that cut down on gun violence?

So that is the basis of the—and we can provide, again, as I say to you, what is in the legislation, the language of the legislation which lays out what the scope and the mission of the resources are for the gun violence prevention research.

And, with that, let me recognize Congresswoman Frankel.

Ms. FRANKEL. Thank you, Madam Chair.

Yeah, I mean, sadly, as we are speaking here today, there is a mass shooting happening right now in California, in San Jose.

Madam Chair, I just want you to know that I actually live in Florida. I don't know if you knew that, but I do.

The CHAIR. I know.

Ms. FRANKEL. There have been so many questions, so, to our guests—thank you very much—if this has been asked, just say, okay, you missed it.

This whole issue of the vaccine passports have been a little controversial, especially in my State where I live, Florida. And I would just like to get your feedback on that, on the use of requiring, you know, vaccine passport to go into certain establishments or cruises or so forth.

Dr. WALENSKY. So the Federal Government has made the decision not to use—not to be the leader in vaccine passports but has said that local communities, the private sector may use it for their industry if they so choose.

I can envision that there would be certain sectors where this would be incredibly helpful. And, for example, cruise ships I think would be one of those, where cruises would like to be able to know the status of the people who are taking the voyage.

What I will say is that the most important thing is that people get vaccinated. And if there are a lot of people who are getting vaccinated, the utility of this passport—in fact, if everybody gets vaccinated, the utility of these passports is nil, right?

So, really, the most important—the reason that we even have to have a discussion about passports is because people are not getting vaccinated. But if we can get people vaccinated, then the importance of these passports really diminishes entirely, or these verification mechanisms really diminish entirely. You know—yeah. I will just stop.

Ms. FRANKEL. Okay. And if you could get us—maybe someone on the staff can get us that confidence hotline number, that would be helpful.

Dr. WALENSKY. I would be happy to do that.

Ms. FRANKEL. I am going to just switch the subject for a moment, and I want to talk a little bit about domestic violence. Because I know that you have a program; I think it is called DELTA. You also manage the Rape Prevention and Education Formula Grant. And I would like to ask you a little bit how that is going, what kind of progress is being made.

Dr. SCHUCHAT. You know, these are such difficult issues for the individuals involved and those who love them. You know, CDC has been developing technical packages, the toolkits of what we know works, the evidence-based, and facilitating that to be used by communities around the country.

And we have funded additional programs to, sort of, scale up these efforts. You know, things are different in one place or another, and sometimes, you know, whether it is rural or an urban area, the nature of the challenges are complex.

The team working on this is incredibly dedicated and empathetic in their carrying out the research efforts, but mainly what we are doing is supporting programs to implement evidence-based strategies.

Ms. FRANKEL. Thank you.

I will give one softball question. I know we have been talking a lot about COVID and AIDS and other diseases and so forth. What, in your opinion, are the top healthcare issues that face Americans today?

Dr. WALENSKY. I am not even a good hitter, but I am going to take a swing.

You know, we need to bolster our public health infrastructure—our workforce, data, our labs.

We need to work on health equity in this country. Everything that we do has to be founded in health equity in this country.

We obviously need to get through this COVID-19 pandemic and get everyone vaccinated.

And, you know, we have a lot of work to do in opioids. We have a lot of work to do in HIV. We have a lot of work to do in mental health. We have a lot of work to do in health losses that we saw during this pandemic. Eleven-point-seven million childhood vaccinations have not been given.

And so I look forward in leading this agency through this pandemic and to address all of the public health infrastructure of this country.

Ms. FRANKEL. Thank you so much, everybody. I am going back to the beaches.

Dr. SCHUCHAT. Wear sunscreen.

Ms. FRANKEL. Maybe this weekend.

The CHAIR. We will get into that issue as well, Lois.

I don't know that there are any other members with questions, because if there are not, what I would want to do is yield to Congressman Harris and recognize you for any closing remarks you would like to make, Dr. Harris.

Mr. HARRIS. Yeah. Thank you very much, Madam Chair.

And, as usual, you know, some of the hearings we have in this subcommittee are the most fascinating hearings, I think, in all of Congress, to be honest with you.

And I want to thank again the doctors for being with us today. I want to say that the CDC, obviously—you know, look, the CDC plays an incredibly important role in the interface between science and the American public to a large extent. The American public looks to leadership in the CDC, grounded in science.

You know, for an example, I am glad to hear that the Federal Government is not going to get involved in vaccine passports. Because we have to admit, there is no data that vaccine passports would contribute anything right now. There is just no data. Now, it might, and it might be tempting to think it would. But it was very tempting to think the fomite transmission was also very, very important at the beginning. It kind of made sense. Look, I used all the hand cleaner in the world. It turns out that is not really as important as we thought. But there is a big difference between making someone carry a vaccine passport and making someone clean their hands with hand sanitizer.

And I think that this is where the difficulty lies in public health and, kind of, treading that fine line between what really will help people and recognizing that there are civil liberties in this country. And that is the best way I can explain it.

And, again, Dr. Walensky, she said, I am more than happy to help staff vaccine clinics, and I have done it. But, in the end, it is an individual's choice to get this vaccine, because it is an EUA; it is not an FDA-approved vaccine. I encourage the vast majority of people I speak to to get it, but, in the end, it is their decision.

And I think the CDC has taken a tremendous step in their mask mandate removal or mask guidance removal for people with vaccines. Because I think that that engenders a lot of confidence in Americans. Finally, a lot of Americans I meet would say, "Wow, yeah, my common sense is, I got in line, I got the vaccine, now I should be able to take my mask off," and now our policies are aligned on that.

And I think that sent a very important signal. I think that is why we are approaching the 70-percent mark in adults being vaccinated. And, of course, you know, that combined with the natural immunity, we should be pretty near herd immunity, and I think that is what the figures are beginning to show now.

So thank you all for the work you do. It is thankless work. As has been pointed out in your testimony, public health officials are underpaid relative to their skill and training. This leads to some problems, there is no question about it. There is no easy solution. But hopefully some of the budget things you discuss for the fiscal year 2022 budget will get us on a better path into getting the public health workforce that we need for the 21st century.

And, again, Madam Chair, thank you again for a fascinating hearing, and I yield back.

The CHAIR. I want to thank Dr. Harris for his comments.

And, I mean, I think I agree, and I—not in a self-serving way, but I think that this subcommittee has the best hearings. And I think, between yesterday and today, there really is—I used the word yesterday "exhilarating." I mean, what we learn, you know, and what both the NIH and the CDC can do to save lives, to keep people healthy in this country is quite remarkable. And I think it is a hallmark of the United States, in terms of our healthcare system.

I am going to just—and I am going to ask both Dr. Walensky and Dr. Schuchat to be absolutely, singularly, like, in a nanosecond: What keeps you up at night?

Dr. WALENSKY. Variants and the concern that people won't get vaccinated and the fact that we are not serving everybody in the country equally.

The CHAIR. Yeah. Okay.

Dr. Schuchat.

Dr. SCHUCHAT. I think we have to remember the rest of the world, and that while it is getting better here, there are many places at risk. So, until we are all out of this, none of us are out of this.

The CHAIR. Uh-huh.

Thank you. Thank you very, very much. Really, I think we covered some very important topics today.

And I just wanted to say this: You know, historically, the CDC has been the trusted voice in leading the response to public health crises. And I will say this—and, look, whether it was Ebola, Zika,

lead poisoning, and so many others. But I think we saw a recent departure from that standard.

So I want to just say a thank you, a real thank you, to both of you and CDC for returning the CDC to be that trusted voice and relying on the science and the data that is necessary to create the confidence in this country that we do have the agency that they can take a lead from. People want to know the truth, they need to be given the truth, and then we could look to how we can direct them.

I would again add that COVID exposed a number of realities in this country. We need a robust public health infrastructure. We can't go back to where we were, and we have to go forward.

So we look forward to receiving the comprehensive President's budget. That is later this week. And then the subcommittee has the challenging task of addressing so many critical issues included in your bill.

And it is remarkable, the range of issues that you look at. We talked about some of them today—you know, maternal mortality. But you do food safety, you do so many other things, you know. And it is immunization and mental health and opioids and HIV, and doing all of that work at the same time of dealing with a pandemic.

So we want to provide the resources that you need, and we will continue to fight for that sustainability that I think has come through as the thread of this hearing today. And that, for the CDC to do the job that we want them to do, you need to have the continued resources, not for just this pandemic, but for whatever else comes to pass for this country.

So thank you.

And, with that, this hearing is adjourned.





WEDNESDAY, NOVEMBER 17, 2021.

## U.S. ROLE IN GLOBAL COVID-19 VACCINE EQUITY

### WITNESSES

**GARY DISBROW, DIRECTOR, BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY, DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**DAVID A. KESSLER, CHIEF SCIENCE OFFICER, COVID-19 RESPONSE**

**LOYCE PACE, DIRECTOR, OFFICE OF GLOBAL AFFAIRS, DEPARTMENT OF HEALTH AND HUMAN SERVICES**

The CHAIR. This hearing will come to order.

As this hearing is fully virtual, we must address a few house-keeping matters. For today's meeting, the chair or staff designated by the chair may mute participants' microphones when they are not under recognition for the purposes of eliminating inadvertent background noise.

Members are responsible for muting and unmuting themselves. If I notice that you have not unmuted yourself, I will ask you if you would like the staff to unmute you. If you indicate approval by nodding, staff will unmute your microphone.

I remind all members and witnesses that the 5-minute clock still applies.

If there is a technology issue, we will move to the next member until the issue is resolved, and you will retain the balance of your time.

You will notice a clock on your screen. That will show how much time is remaining. At 1 minute remaining, the clock will turn to yellow. At 30 seconds remaining, I will gently tap the gavel to remind members that their time has almost expired. When your time has expired, the clock will turn red, and I will begin to recognize the next member.

In terms of the speaking order, we will be going with the chair and ranking member; then members present at the time the hearing is called to order will be recognized in order of seniority; and, finally, members not present at the time the hearing is called to order.

Finally, House rules require me to remind you that we have set up an email address to which members can send anything they wish to submit in writing at any one of our hearings or markups. That email address has been provided in advance to your staff.

And, with that, I want to acknowledge Ranking Member Cole and all of our colleagues for joining this morning.

And a thank you to our witnesses—Dr. Kessler, Dr. Pace, Dr. Disbrow—for speaking with us on our Nation's role in global COVID-19 vaccine equity.

Let me just start by saying that I am disturbed. I am disturbed by the general lack of urgency in ensuring that every person across

the world has access to the COVID-19 vaccine. This pandemic has already sickened 250 million people and claimed more than 5 million lives across the globe. People are dying every day, and, yet, little progress has been made to deliver more vaccines to the countries that are being left behind.

Even as many of us in the United States are receiving booster shots, fewer than 5 percent of people in low-income countries have received a single dose. By some estimates, many people in low-income nations will not have access to a vaccination until 2023 without significant increases in worldwide vaccine production and distribution.

I do sincerely appreciate the work that the Biden administration has done. After all, this administration has been delivering vaccine doses abroad since June. And, so far, United States has donated more vaccines than all other countries combined.

It is also encouraging that President Biden has pledged to donate at least 1.1 billion doses of vaccine by the end of next year while calling for 70 percent vaccination in all countries by fall 2022.

I am particularly proud of the work that my friend, Dr. David Kessler, who joins us here today, has done both during this pandemic and for many years as former Commissioner of the Food and Drug Administration and under the leadership of three American Presidents. I welcome his testimony, and I applaud his commitment to the health and the safety of the people.

I just might add here that I was pleased, Dr. Kessler, to hear the administration's announcement today of a new initiative to invest in domestic vaccine production to increase vaccine by 1 billion doses per year. That is the kind of effort we are looking for, but also wanting to hear is how we are going to accomplish that and how we are going to oversee that distribution as well.

I also want to note the important role that BARDA has played during this pandemic, working extensively to scale up production of everything from PPE and at-home tests to vaccine and therapeutic treatments. I am also grateful that BARDA has used funds provided by Congress to work with COVID vaccine manufacturers, such as Moderna, and that it was BARDA's many years—BARDA's many years of support for mRNA, the platform technology, along with decades of basic research at the NIH that enabled Moderna to produce the COVID-19 vaccine.

And I want to commend the efforts of Dr. Pace, whose Office of Global Health will be instrumental, along with USAID and CDC, in addressing vaccine equity efforts on the ground.

But, on the other hand, it is shocking to me that we have not received full and unfettered cooperation from all of our partners in this effort, including the private companies, such as Moderna, making billions of dollars from U.S. taxpayers.

The fact of the matter is every day low-income countries remain vulnerable to COVID-19 is another day for the virus to mutate and to adapt. And, if we fail to ensure their access to vaccines, those countries will become the breeding grounds for new variants, variants that may be more transmissible or, even worse, vaccine resistant.

I will be blunt. I do not believe we are moving fast enough. Unless we take a more active role in significantly increasing vaccine

production and accelerating distribution worldwide, sharing technology and expertise, and scaling up health system capacity, and strengthening multilateral institutions, we are essentially shooting ourselves in the foot, putting ourselves collectively at the risk of a fifth, sixth, or seventh wave.

We absolutely need to accelerate the production of COVID vaccine by any means necessary, including by invoking any legal authorities at our disposal to compel these vaccine companies to work with partners in the U.S. and throughout the world. Quite frankly, it is not just our moral imperative to ensure the health and safety of our friends across the globe; it is in our own self-interest.

While the United States, as I noted earlier, has donated more vaccines than all other countries combined and has become a powerful leader in the fight to vaccinate the world, why is it taking so long to manufacture the vaccine? Why are we as a Nation being held captive by a botched Trump administration contract, one that allowed Moderna to ignore the involvement of the NIH and benefit from millions of dollars in taxpayer funds?

Just this week, it was announced that Moderna is close to making an agreement to pledge doses to low- and middle-income countries in 2022. This is a positive step forward, but not enough. For the life of me, I cannot understand why we are beholden to this company. People are dying. Time is of the essence. And, in the midst of it all, Moderna is making billions of dollars, controlling vaccine production and negotiations of a lifesaving vaccine that HHS helped them to create.

This is unacceptable. NIH and BARDA must be aggressive in protecting and asserting legal rights to their work. This administration must be aggressive in pursuing every option to work around that botched contract and to use every tool at its disposal to accelerate vaccine production, including the Defense Production Act. And President Biden must be aggressive in compelling other countries to back the TRIPS waiver, which would allow more countries to manufacture more COVID-19 vaccines.

When the World Trade Organization meets later this month for its 12th ministerial conference, I will be watching closely to ensure the proposal on temporarily waiving some intellectual property rights rules under the TRIPS agreement is accepted.

I know these are serious and they are complex issues that cannot be easily resolved, but I also know that failure is simply not an option. This pandemic will not be over until it is over around the world.

I hope that, through this hearing, we can gain some clarity as to why we are not moving fast enough, why we are enabling a system that allows pharmaceutical companies like Moderna to profit off of global suffering and how exactly we plan to vaccinate 8 billion people as soon as humanly possible.

With that, let me turn to my good friend from Oklahoma, the ranking member of the committee, Congressman Tom Cole, for any opening remarks that he may have.

Mr. COLE. Thank you very much, Madam Chairman.

And, just before my remarks, a quick housekeeping piece of advice to you as you preside over. I may have to leave at some point

because of my duties in Rules, so I might not be here at the end, but I certainly am going to stay for as much as possible.

Madam Chair, the United States' investments in biomedical research and medical countermeasures have paved the way for the fastest vaccine ever developed in our Nation's history. These strategic investments led by—with Federal support have also enabled the U.S. to lead the world in vaccine availability. As the President has said, anyone who wants a shot can get one. That is a remarkable achievement, and we are fortunate to be in such a position.

I want to thank the thousands of government and private-sector employees who worked tirelessly to make this reality. Operation Warp Speed, in my mind, remains one of the most undervalued achievements of the last administration.

And I want to associate myself, Madam Chair, with your remarks about the role our country is playing in trying to help other less fortunately situated countries and to get the vaccine as rapidly as possible. I think those are important goals and important questions need to be raised and answered.

And I know we are here today to discuss the United States—what the United States Government can do to bolster global supply of coronavirus vaccines. But, before we delve into that topic, I want to spend a few minutes on a fact that I find deeply troubling.

The Build Back Better legislation introduced in the House contains just \$3,000,000,000 for pandemic preparedness. That is less than 0.2 percent of the total. Let's pause and think about that. Nearly \$2,000,000,000,000 in spending, and just 1.7 percent—that is just less than one-fifth of a percent—is dedicated to preparing for the next pandemic.

Of that amount, less than half is dedicated to funding for public health and preparedness research, development, and countermeasures capacity. Such a *de minimis* amount dedicated to so critical a function should be unacceptable to everyone.

I have said multiple times that you are far more likely to die from a pandemic than a terrorist attack, and, sadly, the results of the last 2 years have shown how devastatingly true that is. I would hope the majority's flagship effort to build a better tomorrow after a global pandemic that has shook the world would recognize the need to invest in a substantial way in biomedical and biodefense research enterprise.

I find this omission another sign of shortsightedness that we see throughout the legislation with short-term extensions and unreasonable policies that most Americans do not support.

I also want to acknowledge, however, that the chair's markup contains six times as much funding compared to the Build Back Better bill, and that is with nearly seven times less money.

Now, while I still believe we need to invest more in biodefense infrastructure, I am pleased to see the levels proposed in the chair's fiscal year 2022 appropriations for this subcommittee. I know our chair strongly supports access to childcare, improving our Nation's schools, and paving a way to affordable higher education for all children.

She also recognizes, in addition to human infrastructure investments, that we cannot neglect the biomedical and biodefense infra-

structure. She supported these programs in her markup, and I hope she sustains that level of support going forward.

We have always found these areas of agreement to serve as the basis for our partnership for 6 years running. I also want to recognize that, in her annual funding bill, she is proposing nearly the same amount of funding as what was put forward in the Build Back Better bill, which covers up to 10 years.

I think this fact shows this subcommittee, possibly more than any other, understands how important these programs are. Underinvestment here ensures the Nation will be less prepared for the next outbreak.

I led with the importance of the continuing investment in biomedical research and programs like BARDA because it was past funding that enabled the United States to be in the—be the current leader by far in global COVID vaccination donations. U.S. has donated and delivered more than 235 million doses of COVID vaccines to more than a hundred countries, and I am pleased at the even more aggressive plans that the administration has unveiled in recent days.

In addition to efforts by the Federal Government, vaccine manufacturers have also made commitments to increase production and availability to ensure vaccination becomes a global reality. As proud as I am of our Nation leading the way, United States should not have the sole responsibility for vaccinating the global population. It is a shared problem and a shared responsibility.

In addition, in my opinion, the Department of Health and Human Services should not be responsible for vaccinations abroad. I understand the agency may have a supporting role to the Department of State and USAID, but events over the last 18 months have shown that we have enough challenges domestically for HHS to focus on, and it should not try to achieve objectives beyond its responsibility and capability.

I would like to end by noting that now is the time for us to be looking at opportunities for the next generation of vaccine technology, development of new therapeutics, and more affordable diagnostics. I know some of those efforts are underway, but too much focus has been given to the continuing of the status quo.

If we continue that approach, we will not achieve global vaccination for years to come. We need to look to new technologies to achieve our goal and should not be neglecting those investments now.

I also think we need to expand our focus to future threats. Now is the best time to leverage what we have learned about COVID to begin research into new countermeasures and potential pathogens. We know the devastation that can be caused by a new virus.

We need to do a better job to identify future threats on the horizon and work on mitigation now. Waiting for the next virus to strike and hoping it is far into the future is foolish. The more we shortchange our preparedness today, the less prepared we are when what may be—just for what may be just around the corner.

I want to thank our witnesses for their time today, and I look forward very much to their testimony.

With that, Madam Chair, I yield back my time.

The CHAIR. Thank you very, very much.

And now what I would like to do is to turn to our witnesses: Dr. David Kessler, who is the chief science officer of COVID-19—the COVID-19 response; Ms. Loyce Pace, director, Office of Global Affairs, the Department of Health and Human Services; Dr. Gary Disbrow, director, Biomedical Advanced Research and Development Authority, BARDA, the Department of Health and Human Services.

Our first witness is Dr. David Kessler. Your full written testimony will be included in the record, Dr. Kessler.

You are now recognized for 5 minutes for your opening statement, and welcome, welcome to the committee.

Dr. KESSLER. Thank you so much, Chair DeLauro.

Chair DeLauro, Ranking Member Cole, distinguished members of the committee, I am David Kessler. I am honored to be serving as chief science officer for the COVID-19 response. Thank you for having me here today and for the opportunity to testify before you.

I have the great privilege of working closely with my colleagues from the Department of Health and Human Services—Director Pace, Dr. Disbrow—who are also appearing before you today.

The United States, by far, is leading the effort to vaccinate the world. We have proudly donated more doses than all other countries combined. We will continue and must continue to donate more and more doses.

Currently, we are donating 1.2 billion doses to the world. This includes the U.S. Government's groundbreaking deal to deliver 1 billion donated doses of Pfizer vaccine to countries in need through COVAX. As of today, 250 million donated doses have been shipped to 108 countries. For every one shot we have put in the arm of an American, we are donating about three shots globally.

Because of what you have allowed—because of what you have allowed HHS and USAID to do, we are spending over \$11,000,000,000 on global vaccine supply. And we continue to encourage our international partners to share more doses and expedite the delivery of those already committed.

Today, we are announcing that, to meet short- and long-term needs both domestically and globally, the United States Government is seeking to enter into a historic partnership with one or more experienced pharmaceutical manufacturers to increase the mRNA vaccine U.S.-based production capacity for domestic and global use by at least 1 billion doses annually, not later than the second half of 2022. This will allow us to address the current COVID-19 pandemic and prepare for future pandemic response efforts.

I want to be clear that I personally continue to engage vaccine manufacturers to increase production and availability of vaccines for low- and low-middle-income countries. Chair DeLauro, we share—we share your urgency and the passion to make sure that we are a leader—the leader in making available vaccines for low- and low-middle-income countries.

As part of those conversations, we negotiated a deal with Moderna and the African Union where the United States defers deliveries of 33 million doses, allowing the AU to buy up to 110 million Moderna vaccines at a reduced rate negotiated by the United States.

We also broke through a logjam and brokered a deal between Moderna and COVAX enabling the two parties to reach an agreement where COVAX will purchase, to date, 56 million doses of Moderna vaccine.

Moderna is also retroactively discounting doses already sold to COVAX, all because of the United States Government's intervention. We have told Moderna that we expect them to help fill the remaining COVAX shortfall. We expect that the number of doses that Moderna will make available to COVAX will increase in the next few weeks.

Let me tell you about another step that we took that I think is a first. The United States Government brokered a historic deal with J&J and COVAX to facilitate the first-ever delivery of COVID-19 vaccines to people in conflict zones and other humanitarian settings that cannot be reached by government vaccination campaigns.

The USG and COVAX worked with J&J to waive liability for doses, pioneering a novel legal approach that will allow COVAX to give donated doses to NGOs to administer to people in these conflict zones and other humanitarian settings.

The U.S. also negotiated a path-breaking deal to make 300,000 doses of J&J available to humanitarian workers around the world.

As the Biden administration continues this critical work, we also need the world to do more. We need every other country to step up against this virus like the United States is doing.

Thank you very much, Chair DeLauro. I am happy to answer your questions.

[The information follows:]

THE DEPARTMENT OF HEALTH AND HUMAN SERVICES  
OFFICE of the ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

Testimony before the  
House Appropriations Subcommittee on Labor, Health and Human Services, Education, and  
Related Agencies

Hearing Titled  
U.S. Role in Global COVID-19 Vaccine Equity

Gary Disbrow, Ph.D.  
Deputy Assistant Secretary for Preparedness and Response, Director of the Biomedical  
Advanced Research and Development Authority  
Office of the Assistant Secretary for Preparedness and Response

November 17, 2021



Chairwoman DeLauro, Ranking Member Cole, and distinguished Members of the Committee, thank you for the opportunity to testify today on our efforts to develop, manufacture, and procure safe and effective COVID-19 vaccines. I am grateful for this opportunity to address this Committee and appreciate your continued support for the ongoing response efforts. I want to start by thanking the Biomedical Advanced Research and Development Authority (BARDA) team for their tireless efforts over the last 21 months to develop critical medical countermeasures to address COVID-19.

***Update on ASPR's COVID-19 Response Effort***

The response to the COVID-19 pandemic has required an unprecedented whole of government approach. Secretary Becerra continues to direct the Office of the Assistant Secretary for Preparedness and Response (ASPR) to lead the ongoing coordination of the COVID-19 response across the Department of Health and Human Services (HHS). ASPR programs are working to directly support elements of the response.

Starting with my office, BARDA, in collaboration and partnership with the Countermeasures Acceleration Group (CAG), continues to leverage the supplemental appropriations provided by Congress to support the development of vaccines, therapeutics, and diagnostics to end the COVID-19 pandemic. To date, BARDA has awarded contracts for 77 medical countermeasure projects to aid the COVID-19 response. All of these contract awards are listed on [medicalcountermeasures.gov](https://www.medicalcountermeasures.gov) in detail and include 15 therapeutics, 55 diagnostics, and seven vaccine candidates. Notably, BARDA has placed 1.5 billion doses of vaccine under contract (including a combination of adult primary, booster, and pediatric doses), purchased over 4.88 million doses of monoclonal antibodies, and shipped more than 144 million diagnostic kits.

ASPR has also leveraged the authorities delegated to the Secretary under the Defense Production Act (DPA) to issue 62 priority ratings for United States Government (USG) contracts for health resources, eight priority ratings for USG contracts for industrial expansion, three ratings for non-USG contracts to support the production of resins for both diagnostics and infusion pumps, and the manufacture of closed suction catheters for treatment of patients with COVID-19—all to ensure that private sector partners making life-saving products are able to acquire the raw materials, components, and products requisite to deliver for the response.

Also under the DPA, ASPR is strengthening the industrial base to secure and develop domestic capacity, retool and expand industry machinery, scale production facilities, train workforces, and ultimately supplying the marketplace with products the US needs to contain further pandemic waves. ASPR continues to use critical funding to invest in expanding domestic manufacturing including investments of: \$250M in manufacturing PPE; \$268M in manufacturing of testing consumables; \$14.8M in vaccine raw material manufacturing; \$160M in fill finish capacity; \$65M in vaccine vial manufacturing; \$168M in manufacturing capacity for at home and point of care tests; and, \$53.8M in testing raw materials, with additional funds going out the door every day. Each of these domestic manufacturing initiatives meets current, as well as future, COVID-19 needs and seeks to create or sustain high-value domestic jobs.

***Biomedical Advanced Research and Development Authority Investments and Programs***

ASPR's BARDA continues to support the innovation, advanced research and development, manufacturing capacity improvements, and acquisition of medical countermeasures (e.g., vaccines, medicines, diagnostics, and other necessary medical supplies). Since late January 2020, BARDA has been collaborating with counterparts across the government to continue to identify potential COVID-19 countermeasure candidates and accelerate their advanced development. Even before initial COVID supplemental funds were made available on March 6, 2020, BARDA initiated investments utilizing advanced research and development funding as well as pandemic influenza funding to quickly evaluate existing partnerships to determine promising candidates that could be pivoted to address COVID-19 and immediately made investments in vaccines, therapeutics, and diagnostics.

Beginning in February 2020, BARDA made a series of initial investments targeting a diverse combination of proven platform technologies suitable for rapid development of vaccines and therapeutics. The investments were made as funding became available, and prior to standing up the interagency Operation Warp Speed (OWS, since renamed the Countermeasures Acceleration Group -- CAG) effort. The small initial investments used annual appropriations and existing contract options that BARDA had established specifically for pandemic preparedness, including BARDA's programs in influenza and Ebola. Technology leveraged from these programs for the Federal COVID-19 Response included:

- Sanofi Pasteur's recombinant protein technology and GlaxoSmithKline's (GSK) adjuvants;
- Merck's recombinant vesicular stomatitis virus (rVSV) technology, first supported by BARDA as part of the now FDA-licensed Ebola vaccine ERVEBO;
- Janssen's adenovirus 26 (Ad26) technology that BARDA supported to develop their Ebola vaccine that is licensed in the European Union (EU);
- Regeneron's monoclonal antibody therapeutic technology utilizing their platform that led to the first FDA-approved Ebola therapeutic.

Using the funds provided by the Coronavirus Preparedness and Response Supplemental Appropriations Act, 2020 (P.L. 116-123) signed into law March 6, 2020, BARDA invested \$1.256B in the advanced research and development of Moderna's mRNA-1273 vaccine candidate, supporting clinical trials and manufacturing scale up and validation. Moderna's COVID-19 vaccine was based on their mRNA platform technology, a platform BARDA had been supporting since 2015 for Zika vaccine development and scale up. This collaboration enabled non-clinical development and advancement of the vaccine candidate into expanded clinical studies, support through FDA authorization and expansion of vaccine production in the United States in preparation for large scale production as soon as the vaccine met regulatory requirements.

Going forward, the investments in a mRNA vaccine will support new vaccine production platforms in the future that will improve the efficiency and reduce the timeline to develop vaccines for other biodefense threats and emerging infectious diseases. Platform technologies,

such as the mRNA approach, can provide flexible and rapid response and have many advantages with potential to revolutionize the way vaccines and therapeutics are produced for known and newly emerging threats.

In order to achieve the ambitious goals set out in the American Pandemic Preparedness plan, it is critical that we apply the lessons learned from the current pandemic to continue to leverage platforms, such as the mRNA platform, to prepare against future pandemics. We must fill the gaps associated with advanced research and development, large-scale clinical trials, documented efficacy with antigen/platform combinations, and warm base manufacturing capacity. With the goal of establishing and maintaining a capability to design, test, develop, and authorize use of a vaccine within 100 days, it will be critical to advance vaccine programs through clinical development and commercial scale manufacturing towards licensure before the next pandemic. These activities are essential to demonstrate manufacturability and assess key safety and immunogenicity issues, such as the potential for immune-enhanced disease in target populations. With resources requested in the American Pandemic Preparedness plan, BARDA would coordinate with NIH/NIAID to develop prototype vaccines against the pathogens (or virus families) with greatest pandemic potential and advance up to 20 promising vaccine candidates into clinical studies and manufacturing scale-up.

BARDA would also establish US-based capability to develop and manufacture safe and effective vaccines against known or unknown pandemic pathogens within 100 days of pathogen identification that will leverage platform-based technology such as mRNA-based vaccines. Manufacturing technology platforms that could be applicable across multiple threats would be prioritized to efficiently address as many unknown threats as possible. The initial goal would be to get vaccine candidates to a point where clinical safety and immunogenicity are established, and, commercial scale manufacturing processes have been demonstrated with sufficient vaccine in final containers to respond to future disease outbreaks under an Investigational New Drug (IND) application. Vaccine candidate readiness would be leveraged to demonstrate clinical efficacy in the context of an outbreak response, such as a naturally occurring outbreak. In the absence of an outbreak or pandemic, BARDA would continue to drive these programs so that they may be viable candidates for FDA authorization via the Animal Efficacy Rule or Accelerated Approval pathways.

BARDA understands the importance of delivering lifesaving medical countermeasures quickly, especially during a pandemic, and that the logistical constraints on the current mRNA vaccines have made it challenging to deliver vaccines across the Nation and globally. In 2019, BARDA established the Beyond the Needle program within the Division of Research, Innovation, and Ventures, focused on the development of alternative technologies that aim to transform the paradigm of making vaccines and therapeutics easier to administer and more widely available, without the need for needles, syringes, vials, and cold-chain distribution burdens. Beyond the Needle supports technologies that use alternative routes of administration, such as oral, intranasal, and transdermal patch technologies that involve simplified logistics that enable easier deployment and uptake and can be administered without a trained healthcare professional. This program anticipates bringing to market the most flexible and efficacious modes of delivering emergency drugs and vaccines to more people, in more care settings, with minimal dosing, supply, and logistical requirements. Specifically, Beyond the Needle aims to overcome the

logistics burdens associated with manufacturing, storing, shipping, and distributing needles, syringes, and other ancillary supplies, and with vaccine cold-chain storage and transportation. In addition, this program aims to increase immunization compliance and make vaccines and therapeutics more widely available, especially in resource-constrained settings and during a pandemic or other public health emergency where qualified healthcare professionals are in short supply. The Beyond the Needle program currently supports six individual programs in different stages of development (preclinical to IND enabling) and ranging from oral, intranasal or solid dose formulations, to 3D printer microneedle patches to deliver vaccines.

### ***International Vaccine Donations***

All of the vaccine doses HHS has purchased to date were ordered for domestic use. However, international donations have been made available from amounts that have been in excess of demand once vaccines were available for use. As of November 9, 2021, of the total number of doses ordered, 433,156,393 doses have been administered domestically.

As of early November, HHS/CAG has donated over 130 million doses of vaccine that DoD purchased on behalf of the HHS to foreign countries or to COVAX. Donations by manufacturer follow:

- Moderna: 71,898,480
- J&J/Janssen: 35,628,150
- Pfizer: 19,460,040
- AstraZeneca: 3,412,900

In addition to the 3.4 million doses of AstraZeneca vaccine donated, 1.5 million doses and 2.7 million doses were made available in March to Canada and Mexico, respectively.

The Administration has pledged 500 million Pfizer COVID-19 vaccine doses to be purchased/donated internationally, on top of the 500 million previously pledged.

### **Conclusion**

Thank you again for inviting me to testify before you on efforts within ASPR to support the COVID-19 response. Since its inception, BARDA has entered over 300 industry partnerships, attained 13 years of clinical product development experience, and supported 61 products that achieved FDA approvals or authorizations. BARDA's long standing expertise of accelerating the advanced research and development of candidate diagnostics, therapeutics, and vaccines through to FDA approvals, clearances, licensures and Emergency Use Authorizations, is unmatched across the government and underscores the overall capabilities that we have brought to bear on COVID-19. I look forward to answering your questions and thank you for passing the supplemental appropriations that have aided our overall response efforts. We could not do our job without your partnership and support.

The CHAIR. Thank you for your testimony, Dr. Kessler.

And our next witness is Dr. Loyce Pace.

Your full written testimony will be included in the record, and you are now recognized for 5 minutes for an opening statement.

Ms. PACE. Well, good morning, distinguished members of the subcommittee.

We see the numbers. COVID has caused more than 5 million deaths worldwide, more than half of these in low- and middle-income countries. Vaccination rates in some of these countries are in the single digits. Less than 10 percent of the population of Africa is vaccinated compared to more than 50 percent in North America and Europe. We know this is unacceptable.

So I want to thank you, Chairwoman DeLauro, Ranking Member Cole, and your esteemed colleagues for convening us today to talk about global vaccine equity and the role our government should play in driving that.

Now, two things I want to say upfront. One, this isn't only up to us. It is going to take actors from all over the world—government officials, industry leaders, community organizations, philanthropists, and others—to make this happen. This is why the President convened those very stakeholders this fall and called on them to fulfill their promises and help close the global access gap. He issued this challenge not only for vaccines, but also for treatments, tests, and critical supplies.

Number two, the U.S. is doing its part, playing a lead role and practicing what we preach. At this point, we have donated close to 250 million vaccines to more than 100 countries around the world, both directly and through partners like COVAX, CARICOM, and the African Union. That is millions of people protected from this virus, thanks to our commitments and action.

We have engaged governments and companies in Asia and Africa to expand manufacturing in those regions, and also called for voluntary technology transfer to facilitate those efforts.

Of course, the world needs more, which is why our work continues. We are not letting up. Those of us in the center of this work know what is at stake if we don't follow through. Not only could we face the constant threat of COVID, but we could continue to burden our health workforce, supply chains, and overall society with an ongoing and seemingly never-ending pandemic.

Not only are our efforts practical; they are personal. We read the same headlines you do, and we hear those accounts ourselves every day. Many of us have lived and worked in countries still lacking what they need. Some of us have friends and family there, managing an unsettling reality and all-too-common stories of persistent health disparities.

HHS staff take calls from colleagues around the world, partners with whom we have worked for years, describing what life is like without access to vaccines. Those are tough conversations, recognizing how great the demand is worldwide. But they are easier when we can offer help, and we do.

Our staff meet with ministries of health about their national vaccination campaigns and how to maximize the supply they receive. We have engaged foreign regulators and researchers so that more product comes to market when and where it is needed. And we

have worked with policymakers from Africa to Asia to Latin America and the Caribbean on real-time responses throughout this crisis, helping to establish or reinforce health surveillance systems and essential services required to succeed.

So, when Kenya or Mexico needed vaccines, they reached out to us. And, when Brazil or India found themselves in crisis, it was the same. Whether working through country-based health attaches, our hundreds of international staff focused on global health security, or contacting the Secretary directly, governments around the world look to HHS for solutions to their public health problem. That has been as true in this pandemic as any other time.

Our track record speaks for itself, built on decades of international relationships and programs that have been tested through multiple health crises, like Ebola, Zika, and HIV. We know how to get this right, and we can do this together. It is in the spirit of partnership that is critical to showing up in the world in a way that matters.

From day one, the President has talked about the importance of international cooperation as part of our COVID response. Similarly, his administration is committed to using equity as the guiding principle for these efforts, but, while ensuring we address health disparities across borders, we must also do so within countries.

We know from our own American experience how vital it is that lifesaving innovations are available to those who need them. Otherwise, we are all at risk. I want to be able to tell a different story, one that has countries not in the tenth percentile but meeting our global goal of 70 percent coverage for COVID vaccine; a world focused on getting back to life rather than fearing another variant or worse.

I want us all to feel safe again and to remember this time as a moment when we did right by one another. We have both a strategic imperative and a moral one to deliver what we can where we can, working to end this pandemic once and for all.

[The information follows:]

THE DEPARTMENT OF HEALTH AND HUMAN SERVICES  
OFFICE OF GLOBAL AFFAIRS

Testimony before the  
House Appropriations Subcommittee on Labor, Health and Human Services, Education, and  
Related Agencies

Hearing Titled  
U.S. Role in Global COVID-19 Vaccine Equity

Loyce Pace, MPH  
Assistant Secretary for Global Affairs

November 17, 2021

## Introduction

Thank you, Chairwoman DeLauro, Ranking Member Cole, and distinguished Members of the Committee. It is my pleasure to represent the U.S. Department of Health and Human Services (HHS) and the Office of Global Affairs (OGA) before your committee today to discuss the role of the United States in global COVID-19 vaccine equity.

The global COVID-19 response is a whole-of-government effort. As the country's health agency, HHS leads the interagency in providing technical expertise on public health, research and development, and associated regulatory issues. We have also helped countries prepare for, implement, and evaluate COVID-19 vaccination efforts, drawing on our long-standing relationships with ministries of health throughout the world.

The COVID-19 pandemic has caused more than five million deaths worldwide, more than half of these in low- and middle-income countries. Through the extraordinary efforts of our colleagues at HHS and across the U.S. government, we have made enormous progress in vaccinations. However, even as we make progress here at home, we know that our ability to end this pandemic depends on making progress around the world.

## Role of OGA

OGA represents the Department in global matters relevant to health, and our programmatic and regional teams engage and represent the United States on health matters in critical global forums and partnerships such as the G7, G20, QUAD (i.e. Australia, India, Japan, and the United States), Association of Southeast Asian Nations, Caribbean Community and Common Market, and Africa CDC. In addition, OGA leads the U.S. government on engagement with the World Health Organization. OGA serves on the Access to COVID-19 Tools Accelerator (ACT-A) Facilitation Council, which serves to guide actions across the vaccine, therapeutics, diagnostics, and health systems and response pillars of ACT-A.

Our HHS Health Attachés, based in strategic posts worldwide, have played and will continue to play a critical role in this pandemic. HHS Health Attachés represent the United States in policy negotiations that touch on the intersection of health, and act as a resource for representatives of other U.S. agencies. They have forged long-standing and trusted relationships with colleagues at our counterpart Ministries and at the World Health Organization (WHO), and have been instrumental in our global COVID-19 response efforts. For example, our Health Attachés in Brazil, India, and Mexico have ensured both U.S. Food and Drug Administration (FDA) and local regulators are at the negotiating table to spur vaccine authorizations. Similarly, they have also linked the Office of the Assistant Secretary for Preparedness and Response (ASPR) and Centers for Disease Control and Prevention (CDC) with their counterparts to understand emergency needs and related support. COVID-19 has reinforced the importance of global partnerships, and the HHS Health Attachés are critical to forging enduring relationships, building technical capacity, and ensuring sustained strategic dialogue with key partners.



### Global Vaccination Commitment

President Biden announced ambitious targets to accelerate global vaccination at the Global COVID-19 Summit in September, with an emphasis on health equity. This includes supporting the WHO goal of at least 70 percent of the population fully vaccinated with quality-assured, safe, and effective vaccines in every country and income category by mid-2022. This announcement was backed by the United States' commitment to deliver 1.1 billion vaccine doses to where they are needed most, with no strings attached. And the United States continues to build on its commitments – only last week, Secretary of State, Anthony Blinken, announced a partnership with Johnson & Johnson (J&J) to reach people in conflict zones and other humanitarian settings that cannot be reached by traditional government-sponsored vaccination campaigns.

In the midst of the pandemic, the United States has demonstrated its global leadership, and we are actively working with other countries, international organizations, the private sector, philanthropic organizations, and civil society to deliver on the President's commitments.

I am proud to report that the United States has donated more vaccines worldwide than any other nation. To date, we have donated more than 225 million COVID-19 vaccine doses to more than 100 countries and economies. This progress is the result of sustained, concerted, and collective interagency action, which includes our colleagues at the White House, the State Department, and the U.S. Agency for International Development, among others.

### Areas for Continued Focus

Critical areas of focus for our continued efforts, which will be critical to our success include: vaccine readiness, vaccine confidence, supply chain, health system capacity, and strengthened multilateral institutions. To date, only about 4 percent of people in low-income countries have received at least one dose of vaccine. About 10 percent of the population in Africa is vaccinated, compared to the more than 50 percent in North America and Europe. We know this is unacceptable. International leaders must accelerate vaccine production, increase donations, and fulfill their pledges to COVID-19 Vaccines Global Access (COVAX), the vaccines pillar of ACT-A.

We have witnessed the challenges of enduring global inequity as the majority of vaccines, therapeutics, and diagnostics have remained in higher-income countries. Let me be clear – this is not a zero-sum-game. As we have learned from previous global health challenges -- from HIV to H1N1 to Ebola, and now again with COVID-19 -- no one is safe anywhere until all of us are safe everywhere.

Without concerted global action, there will be additional cases, illness, and death of people in the U.S. and throughout the world. If we do not accelerate global vaccination efforts, we remain under constant threat from new and emerging variants. Additionally, urgent action is also needed to increase access to diagnostics and therapeutics, and to strengthen the ability of countries to use these tools to save lives now and preserve capacities in health systems to respond. So long as COVID-19 remains a public health threat, health systems worldwide remain at risk of being overburdened, threatening access to basic services such as routine immunizations and antenatal care as well as causing supply chain disruptions for essential health products. We

will also continue to see disruption in other sectors, including the domestic and global economy. Vaccinating the world is a strategic, and more importantly, moral imperative.

Advancing equity has been a cornerstone of this Administration's overall agenda – our efforts in the global health space are no exception. As we continue to respond to the global COVID-19 pandemic, we must think critically about how to prioritize and strengthen health equity between and within countries – not only focusing on the distribution of vaccines and therapeutics, but also exploring ways forward on expanding regional and local manufacturing capacity building, facilitating voluntary technology transfers on mutually agreed terms regardless of income status, strengthening global governance mechanisms, and building more resilient health systems.

And our multilateral institutions, including WHO, must be strong, which includes its regional offices such as Pan American Health Organization in the Americas and the Western Pacific Region. Areas of current focus for WHO are strengthening overall global health governance, existing international instruments, and beginning a dialogue on elements of a new instrument on pandemic preparedness to ensure we are able to mitigate the impacts of a future pandemic threat before they become catastrophic. Discussions are underway and HHS's continued leadership role on these issues will be instructive as Congress considers legislation related to pandemic preparedness and future threats.

### Conclusion

Thank you for your attention and support to continue to champion, amplify, and mobilize global efforts in Congress.

Enduring political will, ensuring sufficient resources, strengthening global partnerships and institutions, sharing innovations, and advancing health equity will put us on a more secure path toward ending this global pandemic, and preventing the next one. Thank you to the committee and my fellow panelists, and I look forward to your questions.

The CHAIR. Thank you. Thank you very much.

Our next witness is Dr. Gary Disbrow. Your full written testimony will be included in the record.

You are now recognized for 5 minutes for your opening statement. Thank you.

Mr. DISBROW. Chairwoman DeLauro, Ranking Member Cole, and distinguished members of the committee, thank you for your—the opportunity to testify today on our efforts to develop, manufacture, and procure safe and effective COVID-19 vaccine.

I am grateful for the opportunity to address this committee and appreciate your continued support for the ongoing response efforts. I want to start by thanking this committee for the funding and support provided to BARDA over the years and during this pandemic, and the entire BARDA team for their tireless efforts for the last 21 months to develop critical medical countermeasures, or MCMs, to develop—address COVID-19.

BARDA continues to play a critical role in the development of vaccines, therapeutics, diagnostics, and other supportive efforts to bring forth these lifesaving medical countermeasures. BARDA has invested over \$49,000,000,000 to develop and procure products to address COVID-19, \$33,000,000,000 in vaccines, \$16,000,000,000 in therapeutics, and over \$500,000,000 in diagnostics.

To date, BARDA had supported the delivery of over 556 million doses of vaccine, and over 443 million doses have been administered; the delivery of over 3.3 million treatment courses of therapeutics; and over 168 million diagnostic tests.

BARDA has been proactive in engaging with our stakeholder communities since the very beginning of the pandemic, to include holding an industry call in January of 2020 with over 1,500 participants. In that same month, BARDA established an MCM portal to act as a single point of entry for parties interested in working with the U.S. Government.

To date, BARDA has received over 4,500 submissions to the portal, and interagency representatives have met with over 670 companies, providing transparent feedback and guidance. BARDA made initial investment to jump-start the development of MCMs utilizing annual appropriations under advanced research and development and pandemic influenza funding.

We received—we have reviewed our portfolio of partnerships and identified proven technologies that could quickly pivot to develop COVID-19 products. These initial investments and additional investments made once supplemental funds were provided laid the groundwork for the portfolio of products supported under Operation Warp Speed and now the Countermeasure Acceleration Group, or the CAG. The CAG has been able to support development of one licensed vaccine, two vaccines granted emergency use authorization, two vaccines that have positive phase 3 efficacy readouts, and one vaccine that is completing a phase 3 efficacy trial.

Vaccines are now available for primary series, booster doses, third doses for immunocompromised individuals, adolescents, pediatrics 5 to less than 12 years of age, and studies are ongoing for pediatrics ages 6 months to less than 5 years of age.

Development was accomplished in 11 months, providing safe and effective vaccine, and represents the best of what the U.S. Govern-

ment and industry can do when we work together. Moving forward, these unprecedented collaborations will be critical to better prepare the U.S. and the globe for future pandemic threats.

BARDA supported the collaboration between Johnson & Johnson and Merck to enhance production capacity announced by the President. BARDA provided funding to Merck to modify one of their manufacturing facilities, a fill/finish facility, and a storage facility to expand domestic production of the J&J vaccine for their international effort.

In addition to the direct support for development of vaccine candidates, BARDA has worked with the International Development Finance Corporation, providing technical expertise for their global investments to expand manufacturing capacity for vaccines.

BARDA initiated efforts to expand domestic manufacturing capacity for the critical components that are necessary to support population-scale manufacturing of vaccines.

BARDA has been provided \$2,600,000,000 under the American Rescue Plan Defense Production Act to expand capacity for raw materials, consumables, fill/finish capacity, needles and syringes and vials. Expanding production of these vaccine components is critical to support expanded domestic and global vaccine production.

As David mentioned, the administration is committed to donating over 1.2 million doses of vaccine. Under HHS CAG efforts, over 133 million doses have been already donated, and an additional 500 million doses are being donated under the USAID–JPEO contract. BARDA and JPEO are in discussions for an additional 500 million doses of Pfizer vaccine to be purchased in a not-for-profit price for donation.

As David mentioned, we recently modified our contract with Moderna to support Moderna’s commitment to making vaccine available to the African Union at a not-for-profit price.

Thank you again for inviting me to testify before you on efforts within ASPR and BARDA to support the COVID–19 response. I look forward to answering your questions and working with my team at BARDA and our colleagues across HHS and DOD to end this COVID–19 pandemic.

Thank you.

[The information follows:]

THE DEPARTMENT OF HEALTH AND HUMAN SERVICES

Testimony before the  
House Appropriations Subcommittee on Labor, Health and Human Services, Education, and  
Related Agencies

Hearing Titled  
U.S. Role in Global COVID-19 Vaccine Equity

David A. Kessler, M.D.  
Chief Scientific Officer  
COVID-19 Response

November 17, 2021

Chair DeLauro, Ranking Member Cole, distinguished Members of the Committee, I am Dr. David Kessler, and I am honored to be serving as the Chief Scientific Officer for the COVID-19 Response. Thank you for having me and for the opportunity to testify before you today, provide this update, and discuss our planned actions and priorities going forward as they relate to the global COVID response.

It is important for Members of this Committee to know that today, there is one COVID-19 Response team that is coordinated throughout all levels of government. We are all part of that team. I have a long history of government service and I can tell you that the COVID-19 domestic and international response is an extraordinary level of coordination, focus, and commitment across our government and the globe.

Before diving into the topic of this hearing, I want to acknowledge up front the important work that was done to bring a vaccine to the American people in record time. Today, the United States is in a special position, with three vaccines authorized or approved for the prevention of COVID-19. I am pleased to report that, according to data from the Centers for Disease Control and Prevention, we have reached 80 percent vaccination levels of at least one dose for people 18 and older and 69 percent vaccination levels for fully dosed persons in this age group.

As we advance new plans to deliver vaccines and therapeutics not only to Americans but also around the world, I have the great privilege of working closely with my colleagues from the Department of Health and Human Services, Director Pace and Doctor Disbrow, who are also appearing before you today.

President Biden and Secretary Becerra have made ending the global COVID-19 pandemic our number one priority. We know that this virus has no borders. Vaccinating Americans and vaccinating people around the world is not a choice. It's an imperative. That's why the US government is doing both.

The President set forth global targets at the Global COVID-19 Summit earlier this year and called on partners to assist with addressing COVID-19 around the world. The United States by far is leading the effort to vaccinate the world. We have proudly donated more doses than all other countries combined. We will continue to donate more and more doses.

While ambitious, the President's global vaccine targets are what we need to get on course for ending this pandemic and with it, the risk it imposes on our countries, communities, health and livelihoods. Led by the U.S., the global community aims to fully vaccinate 70% of the global population with safe and effective COVID-19 vaccines. 5.6 billion doses would be required for 70% coverage in these low and lower-middle income countries, of which 2 billion have already been administered. The time is now to vaccinate the world and save lives To defeat the COVID-19 pandemic, we must work together in pursuit of a shared vision.

Today, I am here to share with you the latest information on vaccine purchase contracts and donations and to discuss some of the global challenges we need to address.

As stated in my opening, the United States has donated more vaccines than all other countries combined. We're donating 1.2 billion doses to the world. This includes the US government's groundbreaking deal to deliver 1 billion donated doses of Pfizer vaccine to countries in need through COVAX. More than 240 million donated doses have already shipped to 108 countries. For every 1 shot we have put into the arm of an American, we are now donating about 3 shots

globally. And we continue to encourage our international partners to share more doses and expedite the delivery of those already committed

I want to be clear that I personally continue to engage vaccine manufacturers to increase production and availability of vaccines for low- and low-middle income countries.

As part of those conversations, we negotiated a deal with Moderna and the African Union (AU) where the United States defers deliveries of 33 million doses, allowing the AU to buy up to 110 million Moderna vaccines at a reduced rate negotiated by the U.S. We also broke through a logjam and brokered a deal between Moderna and COVAX, enabling the two parties to reach an agreement where COVAX will purchase, to date, 56 million doses of Moderna vaccine. Moderna is also retroactively discounting doses already sold to COVAX – all because of USG intervention. We expect that number will increase in the next few weeks. And, under the leadership of President Biden and Secretary Becerra, we continue to scale manufacturing, and invest in vaccines abroad.

Specifically, we have been supporting this expansion with:

- Our Quad partnership with India, Australia, and Japan which is on track to produce at least 1 billion vaccine doses by the end of 2022.
- Our work to expand vaccine manufacturing in South Africa to produce more than 500 million single-dose regimens in Africa for Africa.
- We continue expanding the existing manufacturing footprint at Pfizer; forging novel partnerships like the J&J/Merck marriage. This will result in billions of doses.



- We invested \$2.7 billion of the funding in manufacturing of critical inputs for the vaccine production process and for expanded fill finish lines at factories.
- Our support for an intellectual property waiver.

Additionally, the United States has worked to get doses into arms of some of the world's most vulnerable people. The USG brokered a historic deal with J&J and COVAX to facilitate the first ever delivery of COVID-19 vaccine to people in conflict zones and other humanitarian settings that cannot be reached by government vaccination campaigns. The USG and COVAX worked with J&J to waive liability for doses, pioneering a novel legal approach that will allow COVAX to give donated doses to NGOs to administer to people in conflict zones and other humanitarian settings. The U.S. also negotiated a pathbreaking deal to make 300,000 doses of J&J available to humanitarian workers around the world.

As the Biden Administration continues this critical work, we also need the world to do more. We need every other country to step up against a virus like the United States has.

I look forward to working with Members of this Committee as we address the issues I have highlighted. Thank you for the opportunity to testify today on our recent global COVID-19 Response actions.

The CHAIR. Thank you all very, very much for your testimony.

We now will move to questions, and I will start with the questions, and I would just—and the questions—these are a question, Dr. Kessler, and a couple of followups, but all of which I will mention at what time and—at one time in the interest of time.

I will be frank, and you know that I am. We have dealt with each other before. The irresponsible, monopolistic behavior of Moderna is infuriating. Moderna has made billions in profits through an arrangement gifted to the company by the prior administration, by the Trump administration, and the company's refusal to recognize NIH's role in the development of the vaccine.

Further, Moderna has refused to cooperate, lend its expertise to partners that could increase production of its vaccine by hundreds of millions of doses. That is unacceptable.

So my questions are: Why is Moderna able to limit production of a vaccine that U.S. taxpayers spent billions of dollars to develop and manufacture?

What is the administration doing to compel the company to increase production as well as distribute the vaccine at a reduced cost to low-income countries?

How is the administration going to guarantee that Moderna meets all of its commitments?

Should NIH scientists who were involved in developing Moderna's vaccine be listed on the principal patent application as coinventors, and should NIH receive coownership interest in the vaccine?

Dr. KESSLER. Chair DeLauro, the government's position is that mRNA-1273, the Moderna vaccine, was coinvented by government and Moderna scientists. However, Moderna has so far refused to name the government scientists to the principal patent application. Omitting NIH inventors from the principal patent application deprives NIH of coownership interest in that application and the patent that will eventually issue from it.

With regard to your questions about what we have asked Moderna to do and what we expect, we have gone to the extent of actually calling in and discussed this with the chair of the board of Moderna, members of the board, as well as the senior management of Moderna. Very explicitly, we have asked Moderna to do four things.

One, we have asked them, in the short term, now—not wait quarters from now—but to provide the African Union with doses. To their credit, they have stepped up. And, with our colleagues in the African Union and through the fact that the United States basically deferred our doses so the doses could go to the African Union, that is happening.

Number two, we have told Moderna that we expect them to help fill the supply gap with COVAX at not-for-profit prices with significant doses. We will hear, I expect, over the next several weeks the result of those discussions that are currently underway between Novavax and Moderna.

Number three, we have commitment from Moderna to build a plant—to build manufacturing capacity on the African Continent. That is very important to us.

Chair DeLauro, you know I chair the Elizabeth Glaser Pediatric AIDS Foundation. We have been with you for 30 years. We have worked on the continent in HIV, and I understand, if there is a manufacturing capacity on that continent, that continent will not be last in line. It is just that simple. We have Moderna's commitment. We will see what their followup is.

Lastly, as we testified this morning, we have asked all manufacturers with experience in mRNA to help us expand that capacity for both global and U.S. needs, for both pandemic and for COVID, and we would like Moderna's assistance in there.

A lot to be done. We are watching closely. The President is watching closely. These needs are absolutely essential.

The CHAIR. Thank you.

And I have just a short period of time remaining, but I need to ask the question: The NIH scientists, as you offered at the outset, that there was a coinvention. Are we going to have them labeled and listed as principal patent application as the coinventors, and thereby getting coownership interest in the vaccine, which, as you know, opens the door to the U.S. being able to deal with some of these issues?

So just—I really want to know. If I can very, very quickly, what is our guarantee that that is going to happen?

Dr. KESSLER. That is the United States Government's position, Madam Chair.

The CHAIR. Okay. I will get back. Just—and I want to be able to guarantee. And you said that we have a way in which we can talk about further of guaranteeing that Moderna meets all of the commitments that it has made, so thank you.

Thank you, and let me now yield to Ranking Member Cole.

Mr. COLE. Thank you very much, Madam Chair.

Dr. Kessler, I just actually had some questions that are informational to help me and hopefully the committee get a better idea of the task in front of us.

How much funding remains for the purchase of additional doses for the U.S. population, either booster shots for adults or for children?

Dr. KESSLER. Ranking Member Cole, just how much money remains?

Mr. COLE. Yeah.

Dr. KESSLER. Can I just ask you to repeat your question?

Mr. COLE. Yeah. I am just curious what we may need to do going forward, how quickly we need to do it?

Dr. KESSLER. So we have assured adequate supply for boosters for all Americans, and that is also true for adolescents and children. Obviously, you know, the question beyond that, you know, variants, I always try to stay one step ahead of where we are. But the good news is we really, through your help, right—I mean, this is—this should not be understated. Okay? We could not have done what we have done in providing primary vaccines, boosters, adolescents, now school-age children, without this committee's help—

Mr. COLE [continuing]. You are kind for saying that.

Dr. KESSLER. That was essential, and we have done that.

Mr. COLE. Well, you are kind to say that. I share your opinion. This committee, I think, has done an exceptional job under our chairman in this regard.

How about—let me ask—switch now. How much funding remains for the purchase of international vaccines, which I know you are really focused on? And, again, what do we need to look at going forward there to fulfill the commitments that our country has made?

Dr. KESSLER. Let me, if I may, Ranking Member Cole, let Director Pace answer that question.

Mr. COLE. Of course.

Ms. PACE. Well, thanks for this question.

It is our understanding that we have the funding available to fulfill the President's commitment of the additional 500 million Pfizer vaccines. Beyond that, additional funds through the American Rescue Plan are being utilized towards vaccine readiness and ensuring those shots get into arms once they are delivered.

Mr. COLE. Terrific. This may be more appropriate to you, Dr. Pace. I will let you guys decide who is the best person to answer the question. I trust your judgment.

I am curious, of what we have committed, how much has been distributed? And I know there is a lot of logistical problems involved in a distribution effort like this. So, if you would address that a little bit, too, because I know it is going to impact the speed with which you can get what you have out the door literally.

Ms. PACE. Of course. I can try and address some of this, and then defer to my colleagues. And so, with this initial tranche of 500 million Pfizer doses that is being—that has been procured and being distributed by our partners at USAID, we have 100 million that has gone out. There will be some—an additional 100 million, we hope, by the end of this year, and then tracking towards finishing that tranche in the first quarter of next year, followed by the additional 500 million that the President committed at the summit back in September.

And I defer to my colleagues for anything I might have missed in that regard, Congressman.

Mr. COLE. Do either of you have additional information you would like to provide?

Mr. DISBROW. Yeah. Ranking Member Cole, this is Gary Disbrow from BARDA.

So, in addition to the USAID doses that Director Pace mentioned, for vaccine that was purchased by HHS for domestic use, as vaccine supply exceeded the demand, we have also donated over 133 million doses to over 95 countries.

Mr. COLE. Well, I will say—I don't have a lot of time, but I just want to thank all of you for your efforts in this regard, and I would just ask you to keep the committee abreast. I really do worry. We are juggling a lot of balls right now on Capitol Hill. And, looking forward in funding, this is a stream where I don't think anything should ever be at risk either in terms of obviously taking care of our people here, but also fulfilling these very important international commitments. We want to make sure that you have the resources that you need in a timely fashion, particularly given some of the logistical problems I think are involved in, you know,

dealing literally with a global project and conditions that very, very broadly in many places are very, very difficult.

So, with that, Madam Chair, thank you very much, and I yield back.

The CHAIR. Thank you.

And Congresswoman Lee.

Ms. LEE. Thank you very much, Madam Chairman. Thank you, Chairwoman. Thank you so much for this hearing, and to our ranking member, and to all of our witnesses.

I think everyone agrees it is imperative that the United States lead this fight because we won't be able to end this pandemic and Americans will continue to be under threat unless we find a way to assist every country in the world to vaccinate their people.

And I wanted to focus on the equity issues today. And I guess, Dr. Kessler, you mentioned, if there is capacity on the—manufacturing capacity on the continent of Africa, that certainly would be welcome and supported.

But I think—and I guess maybe Dr. Disbrow, you may be able to answer this, in terms of the United States providing the support for the manufacturing of pharmaceuticals on the continent of Africa. I mean, we know that it is going to be—it is a challenge, and so how do we increase vaccine manufacturing on the continent of Africa using United States' leveraging and with the private companies, with the pharmaceuticals? I mean, what could be a plan, or do we have a plan? That is the first question.

And then, to Director Pace, let me just ask you: Less with regard to CARICOM countries and the continent of Africa, last time I looked, it was pretty dismal in terms of the Caribbean, in terms of the numbers of vaccine, the percentages that had been distributed on the continent of Africa and in the Caribbean. And so I would like to find out—and this was about a month ago when I looked at those numbers. It was horrible.

And so what is the problem? What is the bottleneck, and are we getting any better with countries where there are, quite frankly, the descendants of Africa, because, once again, we see the inequities in Black and Brown countries throughout the world?

So I want to know why in the world are we seeing this when, in fact, we are investing so much into vaccine production and distribution?

Mr. DISBROW. Congresswoman Lee, thank you for that question. I will address your first part of your question.

So agreed. And, as David mentioned, ensuring that we have a vaccine manufacturing facility on the African Continent will make sure that those individuals are not last now and in the next pandemic.

As you are aware, BioNTech has made a commitment to building a facility and supporting a facility on the African Continent. As Dr. Kessler mentioned, Moderna has also committed to supporting a facility on the African Continent. And then we are also working with our colleagues at CEPI and WHO and the Gates Foundation, as they want to establish a vaccine hub on the African Continent.

And what we need to do is, even though this is not directed from—I am sorry—funded directly through USG efforts, the funds that have been provided to Moderna and Pfizer to support, either

through vaccine manufacturing—procurement, actually has provided them the funds to, you know, be able to expand and establish these facilities in Africa.

And I think it is important that Gates, CEPI, WHO, and the companies collaborate so that there is a concerted effort to make sure that the vaccine manufacturing facility or facilities that are established in Africa can be sustained in the long run. That is my biggest concern. You know, everybody is, you know, making these, you know, concerted efforts, but we need to make sure it is coordinated so that we can sustain this beyond the COVID pandemic.

Thank you.

Ms. LEE. Thank you.

Director Pace.

Ms. PACE. Yes. Congresswoman Lee, thank you for your question as well.

So, with regards to the Caribbean in particular, sharing your concerns about where they have been in terms of their vaccination. We have been proud to be able to contribute the vaccines that we have, and now we are facing a pivot point, right, where they have received the vaccines, and now we are working closely with them and the Caribbean Public Health Agency and others on readiness and absorption.

One of the challenges honestly is around demand, the same issue we faced in this country when it came to the distribution of vaccines. The availability and accessibility was there, but we still have to work through community engagement and our longstanding programs to ensure that people really lined up for their shots.

Similarly, there are some logistical and operational challenges that we are working across the interagency to resolve, particularly with some of these mRNA vaccines, as you are well aware, and some of the cold chain capacity that is required on the ground.

And then, finally, there are just workforce constraints, particularly as we continue to pull from existing programs, other immunization programs for those vaccinators, and so that presents a challenge as well, not only in CARICOM, but on the African Continent in terms of readiness.

Ms. LEE. So we have the same challenges in the CARICOM countries as we have on the African Continent?

Ms. PACE. Similar, yes, ma'am.

Ms. LEE. We have the CDC in Africa, on the continent of Africa. We don't have a comparable CDC in the Caribbean. You would think that we would see better results on the continent of Africa because CDC is sited there.

Ms. PACE. That is a fair point, Congresswoman, and I appreciate the work that the African CDC has done. And, yet, I think they require additional support from our CDC, from USAID, and others. And so we are working hand in glove with them and the Africa regional office to resolve those issues as soon as possible, and making progress along the way.

Ms. LEE. Thank you very much.

Thank you, Madam Chair.

The CHAIR. Thank you. And just a quick note with regard to that. It really is about not just the vaccine, but it is about the skills development and the skills training that is required and the tech-

nical assistance that is required in terms of capacity building. Those are the critical ingredients I think we need to focus on.

And I want to thank Congresswoman Lee.

Congressman Harris.

Mr. HARRIS. Thank you very much, and thanks—thank you all for appearing this morning.

Dr. Kessler, I have a question. The vaccines—and, as a background, you know, I think what we are talking about is using last year's technology for this year's problems, or for next year's problems. So these vaccines that we are talking about giving to other countries, or enabling other countries to get, these are the leaky vaccines. Is that right?

I mean, it is pretty clear now that this generation of vaccine that we are talking about sending to other countries are leaky vaccines? They—people who get the vaccines can get coronavirus. They can get—maybe it is a variant. Maybe their immunity wanes. Is that true? Is that clear now?

Dr. KESSLER. These vaccines, Congressman—you and I—I mean, over our careers, what, we have—you know, we trained together, I mean, at Hopkins. I think we have seen a lot of vaccine development. I have never seen vaccines developed in as short a period of time that are as effective. I mean, these are remarkably, remarkably effective. No—

Mr. HARRIS. But they are not—

Dr. KESSLER. No new medicine, no therapy is 100 percent effective. You and I know that.

Mr. HARRIS. Sure.

Dr. KESSLER. These are remarkably effective. To think that these are—

Mr. HARRIS. Right, but they are not as effective as we had hoped they would be. I don't think anybody anticipated that we were going to have people get boosters at 6 months, and that, at 6 months—I am just telling you, you know, I talked to people out in the real world.

They were kind of promised that this vaccine was going to be like the other vaccines they have taken. That is, you know, if they have had the disease, they wouldn't have to take the vaccine. You know, if they got the vaccine, they wouldn't have to get a booster in 6 months.

I don't think there is any other vaccine we administer, is that correct, Dr. Kessler, where you get a booster in 6 months? Is that correct?

Dr. KESSLER. Go back to your immunology, your—

Mr. HARRIS. But there are none.

Dr. KESSLER. Our basic immunology passage right. Remember those, sir?

Mr. HARRIS. But there are none.

Dr. KESSLER. Many of these vaccines, if I may—

Mr. HARRIS. Dr. Kessler, I have very limited time. It was a very simple question.

Dr. KESSLER. If I can just answer your question.

Mr. HARRIS. Is there any other vaccine where you need a booster in 6 months?

Dr. KESSLER. There are many vaccines—in fact, majority of vaccines—a lot of vaccines require three doses as primary series, so I would ask you to think about——

Mr. HARRIS. I am talking about a booster—Dr. Kessler, come on. I am talking about a—and this is important here because we not only have to get the doses to Africa. We have to get boosters to Africa.

So let me move on.

Dr. KESSLER. No, no, no, but, Congressman, I think this is very important.

Mr. HARRIS. Dr. Kessler, I am sorry. It is my—Dr. Kessler, I am the one who asks the questions here.

Dr. KESSLER. I understand, but, please, if I may answer the question.

Mr. HARRIS. Well——

Dr. KESSLER. There——

Mr. HARRIS. Madam Chair, could you please direct the witness to let me ask a question of Dr. Disbrow?

The CHAIR. Well, yes. And I will allow you to do that.

Mr. HARRIS. And not have it count toward my time.

The CHAIR. Congressman, no. And I will provide——

Mr. HARRIS. Thank you.

The CHAIR [continuing]. The time. But, Dr. Kessler, answer your question. You will have time to ask Dr. Disbrow a question as well. Dr. Kessler.

Mr. HARRIS. Madam Chair, it is——

Dr. KESSLER. If you will excuse me.

Mr. HARRIS. I have 5 minutes. I have more questions than Dr. Disbrow. I was going to go back to Dr. Kessler. I need to keep—the witnesses cannot filibuster in this.

Dr. KESSLER. You are raising doubts about the efficacy of this vaccine, and that is wrong, sir.

Mr. HARRIS. Oh, I am sorry, sir. Let me tell you, I am a scientist. You are a scientist. Science raises questions about everything. There may be more effective——

Dr. KESSLER. Very important. You are undermining——

Mr. HARRIS. Yes, it is important.

Dr. KESSLER [continuing]. The confidence of the American people——

Mr. HARRIS. There have been more effective vaccines——

Dr. KESSLER [continuing]. And the world in the vaccine, and that is wrong, sir.

Mr. HARRIS. Oh, good. I am glad you have decided what is right and wrong.

Dr. Disbrow, is it true that Florida did not fund the phase 3 trials for molnupiravir, which looks like it is going to be the breakthrough therapeutics? Is that true?

Mr. DISBROW. That is correct, sir.

Mr. HARRIS. So, despite sending BARDA billions and billions of dollars, the decision was made not to fund a phase 3 trial of a drug that now could be made available to millions of people worldwide who get COVID, even maybe from a leaky vaccine or unvaccinated.

So I have got to—I am going to come back to Dr. Kessler. What are you doing as the COVID czar to see to it that therapeutics are



rapidly advanced as rapidly as possible through the FDA, things like fluvoxamine, very cheap, could be widely available, as a second-prong approach, we send vaccines and therapeutics to these other countries?

So if you could answer about therapeutics.

Dr. KESSLER. From day one, therapeutics has been very high on our agenda. We invested \$3,200,000,000. We are the ones, right, that work with Merck and work with Pfizer. NIH developed—wrote the protocol for the Pfizer antiviral that now has where we are seeing very, very important results that are going before the FDA. We are pushing very hard.

I would like to work with you, Congressman, right, to make sure, once FDA has reviewed these data, that antivirals in addition to vaccines, right—complementing, not substituting for vaccines. Vaccines are still one, two, and three on the list, but I want to get a safe and effective antiviral, accessible to all, so we can turn this around. That is what I would like to work with you on, sir.

Mr. HARRIS. Thank you, and I look forward to that.

I yield back, Madam Chair.

The CHAIR. Thank you.

Congressman Pocan.

Mr. POCAN. Thank you, Madam Chair, and to the witnesses. My apologies for the cult-like fervor to discredit vaccines that some people seem to be obsessed about that could cost American lives. I don't get it, but I am not a doctor. I am just a small business owner, so—but I still want to say apologies because it is rather embarrassing to watch this.

My questions are specifically around the distribution, and I think these will probably be for either Director Pace or Dr. Disbrow. Four questions around distribution.

One, cold chain. I had someone who knows quite a bit about this. I believe the country is Zambia, where they are concerned that, as the vaccines go to the proper cold storage, they have talked to some of the folks that are the insurers who put little thermometers in with the product and that they see spikes going to 45 degrees in those cold storage overnight.

I am concerned about how closely we are watching the cold chain aspects and the consistent deliverable nature of power to these, specifically in some Third World countries like Africa.

Two, do we—are we putting enough resources into the human distribution of these vaccines because that is one issue I have heard that could be another factor in some of these especially Third World countries?

Three, are we investing in—by doing this, in some infrastructure so that perhaps whatever we do with this vaccine could turn out to have other positive health ramifications in these countries?

And, finally, four, can you talk a bit about the demographic discrepancies? We have seen that, in many of these countries, far more men rather than women and other populations aren't getting the vaccine. What are we doing in trying to address that?

So I just thought I would put the four questions out there, and whoever wants to answer them, but specifically I think Director Pace and Dr. Disbrow.

Ms. PACE. I am happy to—

Mr. DISBROW. Would you like to go first?

Ms. PACE. Yes, sir. Thank you, Dr. Disbrow. I appreciate that. And thank you, Congressman Pocan, for those questions.

I want to leave time for my colleague to come in. Briefly, I will say one of the things we are trying to do across U.S. Government is build on existing global health programs and platforms, and so we talked about even leveraging the PEPFAR platform. Again, not to put that under a constraint, but to utilize the health workforce, supply chain, and other capacity in place in countries to help speed up the rate of COVID vaccinations.

We are also hopeful, though, to your point, that, by adding additional resources or support to these national vaccine campaigns, that they will then sort of survive into the future and be able to address some of these existing global health programs, and so it is a nice cycle, if you will.

On the point of reaching women or other special populations and subgroups in particular, we know this from other immunization programs that that is key, and so we are focused on those historically marginalized or vulnerable groups certainly in our efforts working with WHO, Africa CDC, or other community-based organizations in particular.

I will say one thing about the cold chain support, which is just to say we are factoring that into our readiness analysis, if you will, in ways that we can provide technical assistance, not only through CDC and HHS, but through USAID, DOD, and others, and so part of this package of technical assistance. That is part of our sort of global vaccination strategy. But it is also why it is critical to think about other vaccines that can come into the picture that don't require the same level of logistics.

Dr. Disbrow, please.

Mr. DISBROW. Yeah. Director Pace, I think you answered the questions very well and completely. I really don't have anything to add.

Mr. POCAN. Can I just follow up, then, on the cold storage, though, because this was from a very, very reliable source, that, you know, in some of this cold storage where the insurance companies actually are gauging the temperatures, because they do for obvious reasons, they are seeing spikes go up to 45 degrees at night.

So how do we know—yes, they might have the right cold storage, but how do we know that the vaccine is still secure at that level? Are we doing extra to ensure they either have adequate power or they are keeping the temperature so that we are not giving a non-useful vaccine to people? I would just like to ask that again.

Mr. DISBROW. Yeah. So I think it is critically important that, you know, we work with the countries that are receiving the vaccine to make sure that they have ample not only primary power but secondary power as well. We had to do this during the 2014–2015 outbreak of Ebola in West Africa. We actually sent people over there to make sure that they had, you know, primary power and backup generators because you have to ensure that the cold chain is maintained to make sure that the vaccine is still effective.

Mr. POCAN. All right. Thank you.

I yield back, Madam Chair.

The CHAIR. Congressman Fleischmann.

Mr. FLEISCHMANN. Thank you, Madam Chair.

I would like to thank the chairwoman and all of the witnesses for their compelling testimony today, for taking this opportunity to highlight our country's role in the global vaccine distribution effort.

We have heard testimony today about the great success of Operation Warp Speed, and I think we ought to really underline success. The previous administration worked diligently with vaccine manufacturers to develop a safe and effective vaccine, and we are still working to administer primary COVID-19 doses and booster to individuals who voluntarily wish to be immunized.

While I think forced vaccine mandates are counterproductive and send the wrong message on immunization, I am happy to note that the domestic production meets current demand in this country, and I think that is something that all of us can be proud of regardless of our branch: the House, the Senate, or the administration.

In regard to the global vaccine distribution, Dr. Kessler has stated in his written testimony to the committee that the United States has pledged to donate more COVID-19 doses than all of the other countries combined, a whopping 1.2 billion doses worldwide. That effort will provide much-needed relief for lower income countries, and I think that is a goal that both of us share on both sides of the aisle.

That being said, I have heard concern from one of the vaccine manufacturers, Moderna, about that effort. And I think this point is very important to be made in defense of Moderna's position. Twice in 2021, the Biden administration requested contractual modifications requiring Moderna to accelerate and prioritize deliveries from its U.S. factories to the United States Government. These were contractual modifications that were made with the government and with Moderna. My question, I guess for Dr. Kessler, is, how could Moderna have supplied more doses to COVAX under these conditions, sir?

Dr. KESSLER. Moderna has the ability to supply the United States and COVAX, in our judgment, with doses that are needed. They certainly have today, Moderna has that capacity, and we hope that they use it.

Mr. FLEISCHMANN. Yes. And it appears that they are trying to do that. But given the contractual modifications that they were faced with, you would agree that that did place additional contractual constraints on them.

Dr. KESSLER. Early on, Congressman, you are exactly right. I mean, I sat there, and the President's position was that it was very important to get Americans the vaccine and to do that, and also the world.

So we have done that. We have plenty of vaccine here. We are donating that. And now it is up to Moderna. And we will see over the next couple of weeks. We have enough vaccine in the United States. Moderna has significant capacity. I hope the deal between COVAX and Moderna gets signed, and let's see.

Mr. FLEISCHMANN. I appreciate your response, Doctor.

And for everyone, I think the United States, all of us, can be proud of all of the manufacturers, including Moderna and the others, for stepping up in unprecedented times. We can look back now and say maybe things should have been done differently. But I

think the United States of America came together, all of us, yourself included, to work towards combating this COVID pandemic.

So as we go through this, Madam Chair, and to the committee, I think sometimes we need to laud some of the people and praise them as we continue to move forward. Because God forbid if we are ever faced with this situation again with another pandemic or epidemic, we want private companies to partner with the government to get to our end goal.

And with that, I yield back in a great spirit of cooperation. Thank you.

The CHAIR. I thank the gentleman.

And I would just say with regard to that, I understand the cooperative relationship between the pharmaceutical companies and the Federal Government.

I just think the pharmaceutical companies, and in this case Moderna, need to acknowledge the very serious role that the National Institutes of Health and the government played in getting its product to the market.

In fact, they hadn't gotten a product to the market prior to the infusion of both capital and technology that resides with the National Institutes of Health, with the three NIH scientists who co-invented.

And so that ought to be acknowledged in a very public way, and they should not—our scientists should not be frozen out of that process.

And with that, let me recognize Congresswoman Watson Coleman.

Mrs. WATSON COLEMAN. Thank you, Madam Chair.

And thank you to all of the witnesses for your testimony.

I want a clarification on a couple of things I have heard.

Number one, we keep referring to 2022. So are you telling me that we are going to be masked and vulnerable even into the second half of 2022? Can I get that from each of you really quickly, yes or no?

I will start with you, Doctor.

Am I being heard?

Dr. KESSLER. Yes, you are, Congresswoman.

Can I just say, just a point of clarification, will we need to be masked and vulnerable in the—

Mrs. WATSON COLEMAN. Yeah, yeah, yeah, in the second half of 2022, because that is a time of the year that has been mentioned a couple of times in terms of having to do these various things to get us where we need to be. I just am trying to understand my future here.

Dr. KESSLER. Congresswoman, I go to bed every night, and before I go to bed, I mean, I look at the numbers for the day. One of the hardest jobs I have when I had the opportunity to brief the President was to be able to project out where we are going to be in 4 weeks, in 8 weeks, and by the end of 2022.

Anyone who tells you they know where we are going to be in 2022, I don't think it is going to be accurate. I think the most important thing is these vaccines—

Mrs. WATSON COLEMAN. Are vitally important.

Dr. KESSLER [continuing]. They will prevent hospitalization and death.

Mrs. WATSON COLEMAN. Thank you.

Dr. KESSLER. You do not have to worry, if you are vaccinated, and as long as you are not immunosuppressed, these are protectors. These prevent hospitalization and death from COVID. That is the key.

And I hope with the antiviral, let's see what the FDA does. And I think we are going to have significant quantities of antiviral.

Vaccines plus the antiviral, it is the first time I can sit here and I am beginning to see a way we can get this under control—not eliminate, not get rid of the virus entirely, but I think we can get this under control.

I am sorry for going on, Congresswoman.

Mrs. WATSON COLEMAN. Thank you, Dr. Kessler. I can talk to you for a long time, I am sure.

So if we can't do better on the continent of Africa and in the Caribbean, and even if we are doing better in terms of total vaccinations and boosters, how does that negatively impact our well-being here?

I guess I am going to give that to Doctor—the representative from BARDA, Doctor—I am sorry.

Mr. DISBROW. Congresswoman, this is Gary Disbrow. I can take your question.

Mrs. WATSON COLEMAN. Disbrow. Dr. Disbrow. I am sorry.

Mr. DISBROW. No, that is fine.

So, I mean, obviously, until everybody is vaccinated, I mean, or the vast majority, the 70 percent set by the administration, that goal, there are potentials for variants to arise.

And so we need to maintain our vigilance, and we need to do everything that we can to make sure that the COVAX commitments are met, that we are working with countries to make sure that their capacity is increased, so that they—

Mrs. WATSON COLEMAN. Dr. Disbrow, I am sorry. I want to interfere because I want to ask two quick questions that can be answered by you or anybody.

Number one is, how many variants are we monitoring now and what is happening in countries with regard to those variants since we are not having access to one of the three or four vaccines that we are talking about?

And number two is, if we are talking about there being a vaccine capacity manufacturing presence on the continent of Africa, are we talking about 2021, 2022, 2023? What are we talking about?

Those are my two questions.

Mr. DISBROW. Sure. I can answer your second question first. The commitments by Moderna and BioNTech are in 2022, calendar year 2022.

For your first question, there is an interagency group called the SARS-CoV-2 Interagency Working Group, which is made up of experts, subject matter experts from across the Federal Government who are working with WHO and GISAID to evaluate, then monitor different variants, variants of concern, variants of interest, and determining, testing those variants against the monoclonal antibodies that we have as well as the vaccines that we have.

Mrs. WATSON COLEMAN. How many are there, do you know, kind of a round number, how many variants we are tracking, monitoring?

Mr. DISBROW. It varies, both as variants of concern, but I am happy to provide that in a written response.

Mrs. WATSON COLEMAN. Thank you very much.

Thank you, Madam Chair. I yield back.

The CHAIR. Congressman Cline.

Mr. CLINE. Thank you, Madam Chair.

I want to thank our witnesses. And I want to thank the committee for working in a bipartisan manner with both the previous administration and this administration to distribute as many vaccines as possible, as many doses as possible through Operation Warp Speed. The development of the vaccine was critical, and its distribution is still ongoing and remains important.

Dr. Kessler, Moderna is the only company to pledge not to enforce COVID-19 IP during the pandemic. Do you support this pledge?

Dr. KESSLER. Yes.

Mr. CLINE. They have also offered NIH co-ownership, including the ability to license IP, covering Moderna scientist inventions made as part of the NIH collaboration. What is the status of that offer?

Dr. KESSLER. I will let the lawyers at NIH and Department of Justice who are handling this respond. I am not part of those discussions.

Mr. CLINE. But it is safe to say they are ongoing?

Dr. KESSLER. Again, let me defer, if I may, to counsel on negotiations with regard to the patent issues.

Mr. CLINE. Okay. Counsel is not testifying today, and so if you could get me that information, that would be helpful.

It is also disappointing that Moderna was not invited to testify today to actually defend themselves against some of the allegations that have been made.

Dr. Kessler, at a recent event by Yale Law School titled "How to Vaccinate the World" you stated it would likely take several years to build vaccine facilities in places like South Africa. And further, these facilities wouldn't be ready in time to help with this pandemic. Is that correct?

Dr. KESSLER. There is to doubt that building manufacturing capability will take several years. We have done that. But saying that, it is still very important because we have to prepare for future pandemics.

That is why we are working very hard and expect Moderna to be able to work with COVAX to get doses now to low- and low-middle-income countries and to the AU, as well as prepare for the future, sir.

Mr. CLINE. Thank you.

Dr. Disbrow, is it true that money that was appropriated in previous COVID legislation for BARDA to assist with the development of COVID-specific vaccines was diverted to NIH for other purposes? I think this was referenced in an earlier question.

Mr. DISBROW. Yeah. Sir, I would have to check with the Assistant Secretary for Finance and Resources for HHS and provide you that in a written response.

BARDA is appreciative of the funds that this committee has provided to them and the investments that you have made.

Mr. CLINE. Okay. If you come to find that it was diverted, do you believe it should have been diverted if it stymies the ability of entrepreneurs and others in their efforts to find other solutions besides an injectable vaccine?

Mr. DISBROW. So I think it is important that across the U.S. Government we continue to look at other technologies, vaccine technologies. I know there is a vaccine that is being developed that is an oral vaccine as well as one that is a nasally administered vaccine, and I think those are all important to be evaluated, especially as we move forward for pandemic preparedness for the future.

Mr. CLINE. I would agree it is important, and, in fact, there are significant complexities involved in manufacturing, storing, and transporting mRNA vaccines.

So you would agree that rather than forcing companies to give up their intellectual property, we should be encouraging them to develop other forms, including oral and therapeutics?

Mr. DISBROW. So, I mean, we work with companies from all different sectors, and we are happy to have those engagements. We have what is called the market portal, the MCM portal, that companies can submit their ideas. And we have a CoronaWatch, TechWatch meeting. If companies are interested in potentially partnering with BARDA, they can submit their ideas to us, and we would be happy to meet with them and have those discussions.

Mr. CLINE. And I understand the portal exists, but why is it that very little advanced developments for next-generation COVID vaccines and therapeutics have gone through BARDA in the past year and a half?

Mr. DISBROW. So the funds that we have been provided to support the priorities under Operation Warp Speed and now the Countermeasures Acceleration Group for vaccines and therapeutics, we have made key investments to bring those vaccines and therapeutics forward.

And as Dr. Kessler mentioned, we have multiple vaccines that are available as well as therapeutics. But we have not yet been provided additional resources for advanced research and development for earlier symptoms.

Mr. CLINE. And it seems to me that the bigger problem isn't that companies aren't sharing their intellectual property or patent, but there are many other considerations as it relates to making vaccines available around the world.

And that is a troubling trend by this administration. Big government solutions, mandates on employers, and a complete disregard for property rights ultimately does more harm than good. So I hope that the Biden administration will reverse course on both of these issues and instead focus on real solutions for the pandemic.

Madam Chair, I yield back.

The CHAIR. Thank you.

Is Mr. Moolenaar back? No.

If not, we will move to a second round of questioning, a second round of 5-minute questioning.

I think while we acknowledge the role of the pharmaceutical companies, we need to continue to really acknowledge the role of the National Institutes of Health and American taxpayers' dollars and the contribution that it makes to developing these vaccines.

Let me ask about the donation of domestic excess vaccine.

Dr. Kessler, the excess vaccines in the domestic supply, can they be donated, dealing with that before there are expiration dates involved?

When I asked this question at an earlier time of USAID, they told me to deal with HHS on this and looking at the chain of custody issues once the vaccine has been distributed.

What steps is HHS taking to reduce the number of vaccines going to waste in the United States? And what are the chain of custody challenges to sending the valuable vaccine where it will be administered both domestically and internationally?

Dr. KESSLER. Chair DeLauro, thank you very much for that very important question. It is something we spend a lot—both I and my colleagues spent a lot of time on.

Number one, what is most important is that the United States will always and only distribute and donate high-quality vaccines. There is no difference between a vaccine that we are donating and a vaccine that I would put in my family's arms. So it is quality vaccines across the board.

With regard to specifically, we spend a lot of time dealing with expirations. The good news is, in circling, we have seen and we have been able to work to extend the expiration date. And certainly no, for example, no Moderna vaccine—there is no expiration of any vaccine that occurs in our possession. We monitor expiration very carefully, and we plan accordingly.

Now, you are right that sometimes—and we have seen this, and it has been enormous efforts for our State colleagues to do the efforts and get everyone who has wanted a vaccine as quickly as possible, vaccines in the arms of American citizens. It is a heroic effort.

But you are right, when you distribute vaccines out in the field, and they keep on going to certain fields, we are limited by our FDA colleagues, correctly, that we can't send vaccines that we can't assure that chain of quality.

So we work very carefully to make sure that the States don't order more than they actually need. So we are on top of this, I promise you, Chair DeLauro.

The CHAIR. And that has to do with the international side of that as well as extending of vaccines that are not going to expire in short order, given that in some places the domestic capacity—the international domestic capacity—is limited. In some countries, it is much more limited than it is in the United States.

So it is that technical assistance that I think we have to be really focused on as well to be able to get them distributed at the appropriate time so we are not wasting the vaccine.

So thank you.

Let me just ask one question. It has to do with our international partners, Dr. Kessler.



The U.S. has donated 250 million doses, more than all other nations combined. Are other G7, G20 countries fulfilling their pledges for vaccine donations to the low- and middle-income countries? What is the U.S. doing to pressure other high-income countries to meet their pledges and with more urgency?

Dr. KESSLER. With your permission, I would ask Director Pace to answer that.

The CHAIR. Thank you.

Director.

Ms. PACE. Thank you, Dr. Kessler.

And thank you, Chair DeLauro.

So I am really glad you asked this. We have really been pressing on this issue ourselves, recognizing it is going to take all of us.

As you said, the G7 did make a commitment to sharing vaccine, half of which included U.S. commitments, but the others coming from those countries, and we have not fully seen those realized. It is one of the reasons the President convened those world leaders in September and at that event pushed those very countries to come through with their commitments.

Following that meeting, and most recently, the Secretary of State, Secretary Blinken, convened foreign ministers as well and reiterated that call to action.

Since then we published—or what has been published—is a dashboard of sorts that shows how countries are tracking toward their various commitments. And so it is a very transparent look at how not only the U.S., but these other countries, including the G7, are doing with their commitment to COVAX.

So now it is online for the world to see, and we are hoping that that also provides some additional impetus for them to take action.

The CHAIR. Okay. Thank you.

Congressman Cole.

Mr. COLE. Thank you, Madam Chair.

And thanks again to our witnesses.

Dr. Kessler, we have talked about lots of ways in which we have tried to help, and it is certainly appropriate to have additional vaccines sent overseas. And some of our companies have offered to build facilities overseas to try and distribute supply.

Probably one of the more controversial things is the idea of intellectual property transfer. Do you have any thoughts about that, whether or not that is effective, whether or not that is wise?

And, frankly, are other countries—because we are not the only vaccines in the world, obviously, there are other countries—are other companies considering transferring intellectual property?

Dr. KESSLER. I think that companies working together, joint strategic partnerships, the voluntary transfer, the voluntary tech transfer, I think we applaud and we are seeing. We are seeing, for example, Pfizer partner on fill/finish in South Africa. There are a whole host of those examples.

The world needs these vaccines. No one company can do it. We need that technology shared. We have a lot to do here.

Mr. COLE. Well, again, there is a difference between companies working together across international lines to meet what we all agree is an incredible need and us forcing companies, mandating them to share intellectual property.

And I just, for the record, I would be very much opposed to that. I don't think that is fair to those companies, and I think it would discourage investment later. That is my personal view. Others may have a different point of view.

So I am curious about your thoughts about that, whether or not that is happening. And, again, we are not the—we don't think they are nearly as effective.

And, again, you may know more about it. I am sure you know more about it than I do. There are Chinese vaccines, there are Russian vaccines, there are other countries that have vaccines in one sort or another.

Are they considering transferring intellectual property, to your knowledge? And, again, it may not be something that is in your purview even.

Dr. KESSLER. I can give you probably the best example that I think we can all applaud and should applaud. We have seen Merck and yesterday Pfizer agree to transfer, in essence, to the Medicines Patent Pool with regard to their antiviral.

That is enormously important. If these antivirals are as effective as I hope they will be, they are going to be important not only to the United States, they are going to be essential to the world.

And generic drugs—I will let my colleagues, Director Pace and Dr. Disbrow, add—but the generic availability of these drugs, it took us, Ranking Member Cole, I mean, it took us several decades to get this right with HIV. You will remember, the Chair will remember the efforts that we went through in the 1990s, finding those drugs and then spending a good decade to figure out how to make these available.

I think the antivirals that we have now, through really heroic efforts, that we may be able to get on the market here in the United States are going to need to be available around the world, and we are going to need to have generics available.

So I think there are tools to do that. I will let my colleagues comment.

Mr. DISBROW. So, Ranking Member Cole, to answer your question, I am not certain if the Chinese companies that are developing the vaccines, Sinovac and Sinopharm, are tech transferring their technologies.

I think it is important, as Dr. Kessler mentioned, for the companies to tech transfer where they can to expand capacity. But I think it is even more important that we are supporting all of the critical components that are necessary to manufacture additional vaccines.

We have to do more than just do tech transfers for drug substance and drug product. We need to make sure that we are expanding capacity for the raw materials, the consumables that are in short supply, the fill/finish capacity that was in short supply even before the COVID-19 pandemic hit, needles and syringes which are going to be necessary across the globe, as well as vials.

So we are making those investments. And, again, I appreciate the funding that has been provided by this committee. We are doing that. The primary investments will be here domestically and to onshore those, but they will not only support domestic manufac-

turing but our global partners who also need those materials as well.

Mr. COLE. Very helpful.

One quick last question, and this is directed at you, Dr. Kessler, but, again, please feel free to share it around.

I am just trying to get a clearer—and you may not be in a position to give it—but a clearer view of the level of funding we need to deal with the problem.

So what do you anticipate HHS needing, and I mean in dollars, for the global COVID response for the next year? My friend the Chair and I will be probably dealing with this at some level when we are negotiating what is the appropriate level of funding next year. Or, I don't know, maybe it is a supplemental, maybe it takes time to get around it.

We all have the same objective here. I think owing or having some sense of what the scope of the efforts should be is really important in getting it right.

So your best judgment now, with the caveat you can revise it when you need to, because I am sure it is a pretty complex question and pretty moving target.

Dr. KESSLER. It is a very welcome question, Congressman Cole.

I will take responsibility. You gave us the resources. And I will tell you, we have put those resources to very good use. You see that. That is why we have the vaccines we have today. That is the reason why we can get our school-age kids, it is because of those resources.

But I will tell you, Congressman, I have spent those resources, and we are scratching. Let me let our colleagues, our staffs work together. But it is really because of this committee we got to where we got. And it is not done without real investment by the American people for both the United States and for the world.

And we have spent a lot of dollars, and we are very grateful for that. And if we can work together on that question, I would appreciate it, sir.

Mr. COLE. Yeah, absolutely. And, again, it is absolutely not a critical question, it is just an informational one to try and get to where we are going.

I appreciate what has been done. I think it is an extraordinary effort. I think it is something the country can be proud of and all of humanity benefited from.

So I think you have used the resources we have given you wisely and well. I am just trying to get an idea of what we might need going forward. So we will work on that together.

Madam Chair, thank you very much for your indulgence on the time. I am very grateful. Yield back.

The CHAIR. Thank you.

Congressman Pocan.

Mr. POCAN. Thank you, Madam Chair.

And I am going to follow up on Ranking Member Cole's question, because that was exactly what I was going to ask, and maybe even a little more specifically, to Director Pace.

I know from last month's SFOPs hearing USAID funding is soon to be finished. How much more money are you going to need before

the end of year to accomplish our goals? And are we going to be seeing an additional request from the White House?

I am just trying to get a little better idea, because I completely agree with our Ranking Member, what we have done already has been very important, but I know it is not enough, and you have broader goals than the funding we have given you. I would like to have a little better understanding of what you may need.

Ms. PACE. Sorry. I was trying to get myself off mute here.

Well, like Dr. Kessler said, we very much appreciate this question. And as he also said, we have fully obligated the funds that we have received and graciously so.

One of the issues that we have focused on in this hearing has been the issue of readiness and the fact they are at this pivot point. And so that truly is a focus of our moving forward. Not to say we won't keep our foot on the pedal when it comes to sharing, but we still need to be focused on shots in arms and some of the logistical issues, demand generation, and other areas that you flagged for us earlier, Congressman.

So that is one way we could use additional resources or might use additional resources should they be available.

We also have a cadre of Health Attaches around the world who have been working tirelessly on these efforts for longer than I think they expected. And so sometimes we, because that is not what is in front of us, we don't realize how much man or woman power is sort of powering this engine to allow us to respond effectively worldwide.

So those are just some examples of what has been working or where we would like to lean into our work, but obviously we defer to R&D (ph) to present the case more broadly.

I suppose the last thing I will offer is the idea of preparedness and not forgetting that alongside our response. And I know the Vice President made this announcement at the President's summit committing \$250,000,000 to a Financial Intermediary Fund and furthermore requesting of Congress another \$850,000,000 toward that effort.

And so ensuring we have a balance across response and preparedness will be important for us too. Thank you.

Mr. POCAN. Thank you.

And then one final question for Dr. Disbrow on vaccine access in some difficult places. I know last week the U.S. announced it negotiated a deal to ship additional doses of vaccines like Johnson & Johnson overseas to conflict zones. And Secretary Blinken specifically talked about the need to get that in some of the areas that have humanitarian concerns.

Can you talk a little bit about what technology infrastructure and human resource investments are needed to deliver those vaccines to humanitarian settings? And can you talk a little bit more about that J&J deal, please?

Mr. DISBROW. Yeah. So I apologize. I am going to defer to Dr. Kessler who brought it up in his earlier comments.

Mr. POCAN. I apologize. I am getting the wrong spot. Thank you.

Mr. DISBROW. David.

Dr. KESSLER. Congressman, you are exactly right. This was the first. It may not have been the most doses that we have shipped,

but I will tell you, among many of us, my colleagues, it was some of the most meaningful doses, to be able to get doses to people for whom no government program has ever gone before.

And I want to applaud our colleagues at J&J for working with us. Because we talk about donating doses, it sounds simple, but I can tell you the regulatory, legal, all those things are important because of the safety of this.

So to those humanitarian centers, just absolutely critical and very important.

Mr. POCAN. And is there anything on the actual delivery side you can share with us, specifically more information on this J&J deal? I know you said it may be smaller than we would like, but still extremely significant that this is happening. Can you just share a little more on the details?

Dr. KESSLER. No, the only reason I said smaller than we would like is we tend to talk in tens of millions and billions of doses. And here every 10,000, a hundred, is a big deal. I am not minimizing. I will get you the delivery schedule if I can, if I could submit that to you. I will get you the delivery schedule.

Mr. POCAN. I would love to see that.

I would yield back, Madam Chair. Thank you.

The CHAIR. Thank you.

Mr. Fleischmann. Congressman Fleischmann.

Mr. FLEISCHMANN. Thank you, again, Madam Chair.

And to Dr. Kessler, Director Pace, and Director Disbrow, thank you for your testimonies today and for your very good and candid, informative answers to the committee's questions.

We are all appropriators today, and our oversight questions are so important, not only to the committee, but to the Congress, but to the American people. So I thank you.

I want to touch on a couple of issues that we have touched on before, but really just for clarification purposes more than anything.

Dr. Kessler, do you fear that there is a lack of infrastructure that would safely support independent vaccine manufacturing and distribution in some of these other countries in which we want to help their citizens?

Dr. KESSLER. I will let Director Pace comment in a second.

I do recognize, sir, that getting vaccines delivered is only part of the equation. I think I mentioned I spent a decade chairing the board of the Elizabeth Glaser Pediatric AIDS Foundation.

Some of you will remember Elizabeth. That foundation was started in the U.S. because of her kids becoming infected. And we moved globally very early on to be able to get doses to low- and low-middle-income countries.

That technical assistance, that capacity, that absorption, that uptake, I mean, again, we have more to do on supply. But I think your question is absolutely key with regard to that kind of technical assistance with regard to that uptake.

Director Pace, please correct me.

Ms. PACE. Thank you very much, Dr. Kessler.

I want to draw on something Dr. Disbrow said earlier about the sort of spectrum of needs and technical assistance when it comes to manufacturing capacity in some of these countries and clarify

our sense that it is not only building some of the facilities, if you will, or hubs from scratch, but there is some existing infrastructure there, and it is a capacity on which we might be able to build the various investments the U.S. Government is making.

So in addition to some of the other examples that my colleagues have offered, our Development Finance Corporation, working with the Department of Health and some of our Health Attaches in places like India and South Africa, have identified those locales to sort of again build on existing capacity in a way that can accelerate us getting to scale.

I am not sure if Dr. Disbrow has more to add or if you, Congressman, have additional questions. Thank you.

Mr. DISBROW. In addition to that, Director Pace—and your question is a great question. So it is more than just the facilities. You also have to make sure that you have trained people who can work in the facilities.

And so in some of the countries where they may have not had the experience of manufacturing vaccines and fill injectables, you really need to make sure that you have that, they become very—once they are trained, other companies want to take them away and use them because training and making sure that those individuals are available is very difficult.

But it is more than just the facility, it is also making sure that you have the people and the infrastructure to support it.

Mr. FLEISCHMANN. I sincerely appreciate all three of your answers to clarify that for the committee.

In closing, I would like to say this to everyone involved. It is my hope that these conversations progress in a way that will provide for a solution that continues our humanitarian work while staying sensitive to the protections and the liabilities of U.S. companies.

As you know, I am a champion for the free enterprise system. I think all of the companies involved have done a very laudatory job stepping up at a time of crisis, coming together, working with the government to accomplish the goal of defeating COVID both nationally and internationally.

So with that, I thank you, Madam Chair, and I yield back.

The CHAIR. I thank the gentleman.

And what I will do is to just—I just want to ask one question and then we will close. And if the gentleman would just bear with me because we need the two of us to continue. I think we are the only two left. But I will make my case here.

I will submit for the record questions that have to do with vaccine equity to you, Ms. Pace.

I would love to know about the antivirals, Dr. Disbrow, and I will get this question to you about how BARDA contributed to that development.

And to you, Dr. Kessler, about our negotiations with Pfizer or others or using the Defense Production Act for us to up our production in order until we have 20—while we pledged 1.1 billion doses, only 226 million doses have been shipped, 20 percent or so, and Pfizer is producing the 1 billion. So what is it that we can do to accelerate the pace? And I note that people are working very, very hard at this.

But I will submit those questions.

And if I might just close, and I want to just say a thank you to you, Dr. Kessler, Dr. Pace, Dr. Disbrow. I think we covered important topics today.

I would make one. It would be my hope that we could move on our appropriations bills for 2022 because locked within those bills at the moment are serious, very, very serious resources for the areas that you cover and for the issues attached to this discussion. That would be very, very helpful in your being able to further continue your work.

A couple of points here. The virus exposed a number of our shortcomings in our preparedness, but also our interconnectedness with the world. And so COVID is not just a domestic challenge, it is a global challenge. And the United States needs to contribute to that solution, and we are working at that.

But the longer COVID is allowed to spread, it becomes a breeding ground for new variants that may be more transmissible and that could evade current vaccine.

So not enough vaccine in the world now. Limited vaccine needs to be better. That includes providing as much vaccine as quickly as possible to other countries.

We must also support the efforts to accelerate manufacturing capacity, and that is a conversation with BARDA, to maximize vaccine access and equity as soon as possible.

We have had the discussion about facilitating tech transfers sooner rather than later because in some ways the lack of capacity that some of these countries have. And we have this capacity, but they don't. And we need to help them with that effort.

I would urge you to explore every avenue to continue to exert pressure on those companies that were supported with U.S. taxpayer dollars to accelerate production and distribution of the vaccine. I know some of the companies have been excellent partners. I commend them for their leadership.

I would find it unconscionable for any company to make billions in profits without doing everything in its power to reach the most needy throughout the world. It is not just a moral imperative to ensure the health and safety of billions of people, it is in our Nation's national security interest to bring this pandemic to a close as rapidly as possible to save lives. And we have the power to do that, I might add.

And a final note. It is my hope—and I know that this is not your bailiwick, I am sure you will refer me to USTR—but that we do have a ministerial meeting on the 30th of this month where the issue of the temporary transfer of intellectual property—and I emphasize the word temporary transfer of that intellectual property—will be the point of discussion.

And I want to commend the work that the United States has done already in this area at the last TRIPS meeting and my optimism for what we will do at the ministerial on the 30th.

I just say, all in all, it is so much within our power here in the U.S. to be able to deal with these issues. I thank you for your work, for your life's work, and for what you are doing for all of us now, what you are doing for our country, and what you are doing internationally. Thank you so much for being with us.

And with that, I call this hearing to a close. Thank you all very much.



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