

ARPA-H: THE NEXT FRONTIER OF BIOMEDICAL RESEARCH

HYBRID HEARING BEFORE THE SUBCOMMITTEE ON HEALTH OF THE COMMITTEE ON ENERGY AND COMMERCE HOUSE OF REPRESENTATIVES ONE HUNDRED SEVENTEENTH CONGRESS SECOND SESSION

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ARPA-H: THE NEXT FRONTIER OF BIOMEDICAL RESEARCH

TUESDAY, FEBRUARY 8, 2022

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON HEALTH,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to notice, at 10:34 a.m. in the John D. Dingell Room 2123, of the Rayburn House Office Building, and remotely via Cisco Webex online video conferencing, Hon. Anna Eshoo (chairwoman of the subcommittee), presiding.

Members present: Representatives Eshoo, Butterfield, Matsui, Castor, Sarbanes, Welch, Schrader, Cárdenas, Ruiz, Dingell, Kuster, Kelly, Barragán, Blunt Rochester, Craig, Schrier, Trahan, Fletcher, Pallone (ex officio); Guthrie (subcommittee ranking member), Upton, Burgess, Griffith, Bilirakis, Long, Bucshon, Carter, Curtis, Crenshaw, Joyce, and Rodgers (ex officio).

Also present: Representative Rush and DeGette

Staff present: Elizabeth Ertel, Office Manager; Waverly Gordon, Deputy Staff Director and General Counsel; Tiffany Guarascio, Staff Director; Mackenzie Kuhl, Press Assistant; Una Lee, Chief Health Counsel; Meghan Mullan, Policy Analyst; Juan Negrete, Junior Professional Staff Member; Kaitlyn Peel, Digital Director; Caroline Rinker, Press Assistant; Chloe Rodriguez, Clerk; Andrew Souvall, Director of Communications, Outreach, and Member Services; Asad Ramzanali, Legislative Director; Kate Arey, Minority Content Manager and Digital Assistant; Sarah Burke, Minority Deputy Staff Director; Grace Graham, Minority Chief Counsel, Health; Nate Hodson, Minority Staff Director; Peter Kielty, Minority General Counsel; Emily King, Minority Member Services Director; Bijan Koohmaraie, Minority Chief Counsel, Oversight and Investigations Chief Counsel; Clare Paoletta, Minority Policy Analyst, Health; Kristen Shatynski, Minority Professional Staff Member, Health; Olivia Shields, Minority Communications Director; Michael Taggart, Minority Policy Director; and Everett Winnick, Minority Director of Information Technology.

Ms. ESHOO. Good morning, colleagues. The Subcommittee on Health will now come to order. And due to COVID-19, today's hearing is being held remotely, as well as in person.

I would just like to make a brief statement, and then move on with our hearing.

On the first day of President Biden's presidency, he announced a very high standard in terms of conduct in his Administration. Dr. Eric Lander mistreated subordinates. It is a long record, and I be-

lieve that, because he didn't live up to that standard that the President set, that his resigning was the right thing to do. And so he, obviously, is not here this morning. He resigned last evening, one of our Nation's most brilliant scientists. And so he has stepped down from being the director of the Office of Science and Technology Policy. Again, I think that was the right thing to do. Women are not lesser beings.

For members and witnesses taking part in person, we are following the guidance of the CDC and the Office of the Attending Physician. So we are asking everyone to please wear your mask when you are not speaking.

For members and witnesses taking part remotely, microphones will be set on mute to eliminate background noise. Members and witnesses, you will obviously need to unmute your microphone when you wish to speak.

Since we have some witnesses appearing virtually today, I need to ask my colleagues in the hearing room to mute themselves whenever they are not speaking, so we can clearly hear the witnesses' responses. If there is background noise, it really diminishes the voices of those that are testifying.

Since members are participating from different locations at today's hearing, recognition of members for questions will be in the order of subcommittee seniority.

Documents for the record should be sent to Meghan Mullen at the email address we have provided to the staff. All documents will be entered into the record at the conclusion of the hearing.

The Chair now recognizes herself for 5 minutes for an opening statement. And before I begin that, I want to thank our witnesses this morning for being so cooperative to move your presence up in the hearing, given the absence of and the resignation of Dr. Land-er.

OPENING STATEMENT OF HON. ANNA G. ESHOO, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

ARPA-H, the Advanced Research Projects Agency for Health, presents a unique opportunity to take a major leap forward in biomedical sciences by funding high-risk, high-reward innovation that will improve the quality of life for all.

Let me start by describing where ARPA-H fits by painting a picture of the current landscape of biomedical innovation, which I think of as a tale of two mountains, with a valley in between.

On one end of the landscape, we have a mountain called basic research, which is supported by the National Institutes of Health, a research lab that traces its roots to a 1887 lab in the Marine Hospital Service. Basic research is curiosity-driven, motivated by a desire to expand humanity's knowledge. Discoveries in basic research are the critical building blocks for modern medicine. Everyone on this subcommittee supports NIH. We have worked to strengthen it and fund it, and we take great pride in it.

On the other end of the biomedical innovation landscape is a mountain called applied research. Companies have a profit motive to commercialize scientific discoveries with market potential. Investors take risks in applied research, but only within a narrow band

of what is foreseeable from the industry's perspective. The public depends on private investments to bring biomedical discoveries to market.

In between these mountains of basic and applied research, it is what is called the valley of death. There are countless ideas that have the potential to be breakthrough cures, but the needed investment can't be raised because the risk is too great for private actors and is outside the realm of basic research. ARPA-H aims to turn this sunken valley into a lofty mountain, where breakthrough discoveries can be realized on the deadliest diseases we face.

How will this work in practice? For that answer, we turn to DARPA, which is the inspiration for ARPA-H. In many ways, DARPA mirrors the culture of Silicon Valley, which I am very proud to represent. In the Valley, every successful entrepreneur stands on the shoulders of failed bets that came before them. Investors take many bets within a given area, and then they quickly double down on what works.

This similarity in cultures between Silicon Valley and DARPA is not a coincidence. Many of DARPA's successes happened in the Valley. ARPANET, the precursor of the modern internet funded by DARPA, had one of its four original network nodes at Stanford Research Institute. DARPA also funded major developments in semiconductors made of silicon, the namesake of my region. And DARPA is the source of GPS, which has countless academic and commercial linkages to Silicon Valley.

ARPA-H, as proposed in H.R. 5585, the ARPA-H Act, would be an independent agency within HHS designed to make high-risk, high-reward investments. I have worked on the legislation for several months after the President convened a small group of bipartisan representatives—and bicameral—in the West Wing last March to describe his vision for the agency.

Like DARPA, my legislation proposes ARPA-H to be made up of highly empowered program managers who are not career government employees, but are instead experts in their field who dedicate their time to short-term projects for long-term results. Some of these program managers could be NIH-funded career academic scientists ready to break the mold. Others could be leading computer scientists that build new methods of deploying AI to find discoveries for rare diseases.

I have talked to many members of this subcommittee personally about the legislation to create ARPA-H, and it is my top legislative priority in this Congress, and I welcome your ideas on the topic. So if you haven't expressed them, make sure you do to me.

Let me thank my colleagues, Congresswoman Diana DeGette and Congressman Fred Upton. They have also put a great deal of time and thought into this issue, and I am pleased with their support of the legislation. Their work on Cures 1.0—we hear a continuing refrain about the effectiveness of that—with that legislation that became law, and now their work on Cures 2.0—many scientists have told me that the two bills are complementary, and I look forward to advancing both.

Finally, this hearing was noticed, as we said—as I said at the beginning, as a two-panel, and I want to welcome the panelists that

changed their schedules to be the starting brilliant panel that I know that you are.

[The prepared statement of Ms. Eshoo follows:]

PREPARED STATEMENT OF HON. ANNA ESHOO

Committee on Energy and Commerce

**Opening Statement as Prepared for Delivery
Of**

Subcommittee on Health Chairwoman Anna G. Eshoo

Hearing on “ARPA-H: The Next Frontier of Biomedical Research”

February 8, 2022

ARPA-H – the Advanced Research Projects Agency for Health – presents a unique opportunity to take a major leap forward in biomedical sciences by funding high-risk, high-reward innovation that will improve the quality of life for all.

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In between these mountains of basic and applied research is what’s called the valley of death. There are countless ideas that have the potential to be breakthrough cures but the needed investment can’t be raised because the risk is too great for private actors and is outside the realm of basic research. ARPA-H aims to turn this sunken valley into a lofty mountain where breakthrough discoveries can be realized on the deadliest diseases we face.

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Some of these program managers could be NIH-funded career academic scientists ready to break the mold. Others could be leading computer scientists that build new methods of deploying AI to find discoveries for rare diseases.

I've talked to many members of this Subcommittee personally about my legislation to create ARPA-H. It is my top legislative priority in this Congress, and I welcome your ideas on the topic. So if you haven't expressed them to me yet, please make sure you do so.

Let me thank my colleagues Congresswoman Diana DeGette and Congressman Fred Upton. They've also put a great deal of time and thought into this issue, and I'm pleased with their support of the legislation. Their work on *Cures 1.0* - we hear a continuing refrain about the effectiveness of that legislation that became law - and now their work on *Cures 2.0 Act*, many scientists have told me the two bills are complementary, and I look forward to advancing both.

Finally, this hearing was noticed - as I said at the beginning - as a two-panel hearing. I want to welcome the panelists who changed their schedules to be starting as the brilliant panel that I know you are.

Ms. ESHOO. So, the Chair is now pleased to recognize Mr. Guthrie, the ranking member of our subcommittee, for his 5 minutes for an opening statement.

OPENING STATEMENT OF HON. BRETT GUTHRIE, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH STATE OF KENTUCKY

Mr. GUTHRIE. Thank you, Chair Eshoo, and thank you. I want to associate with your words on Director Lander. Everybody deserves to be respected. Everybody deserves to be respected. And the ones who always think they are the smartest people in the room, sometimes other people are a lot smarter than you think they are, and we need to be mindful of that, and I am just disappointed that—I am glad he is not here today, but, you know, he has answers that we need to—hopefully, the White House will have somebody that can answer the questions as well.

Today we are discussing the proposal creating the Advanced Research Projects for Health, ARPA-H, that would establish a DARPA-like agency housed in the National Institutes of Health. Others and I on this committee have been strong supporters of healthcare innovation, specifically biopharmaceutical and biomedical research, and the great success stories—Operation Warp Speed, which was established by President Trump at the beginning of the COVID-19 pandemic.

I think very early in President Biden's term a group of us went to the Oval Office. I remember being in the Oval Office very early in the term, and we were talking about this, and I made the comment when we left—I don't know if any of you remember—I think I said that people are getting tired of votes going 220 to 215 in the House. People are ready to have agencies and things that we can work on and work on together, and healthcare is something we have always been able to work on together.

And you know, we just—we have seen—we didn't see that, we didn't see bills that were—could generate bipartisan support moving forward, and we want to work together. But there are a couple of questions that we really need to ask, and I had told Dr. Lander before that these would come up, and—because we had a phone call before all of his situation.

And the questions is NIH itself, and one is just the role of a new agency. And there is one point at NIH. Last Congress, as ranking member of the Oversight and Investigation Subcommittee, I co-led a letter to Director Collins of NIH and the Director Wray of the FBI to request information on how their agencies are working to remove foreign influence from biomedical research.

NIH is the largest funder of biomedical research in the world. And Director Wray described how researchers from China can mask their identity to accept millions of U.S. grant dollars to steal U.S.-backed biomedical research to give China a competitive edge. And I know that some of my Republican colleagues have actively led on trying to get other information on grants from the NIH, and we have not been able to move forward. So it makes this more difficult to try to create a new agency that would be part of NIH.

To be clear, I believe these hearings are important, and we need to understand the gaps in care across our healthcare system, and

how an agency like ARPA-H could close these gaps. So we need to—but we do have questions about how this new agency would impact research efforts being led by similar Federal agencies in addition to our private sector partners.

ARPA-H is anticipated to be housed within NIH, whose mission is to conduct fundamental basic research to ensure we have foundational understanding of how biological systems work. But remember the private sector, not NIH, is responsible for bringing the breakthrough therapies to market. Only five percent of NIH-funded research initiatives result in treatments that come to the market, and only yield six new patents for every 100 million spent on research. However, the research is built upon by the private sector to move forward.

And the CBO data further shows the pharmaceutical industry invested 83 billion in research and development in Fiscal Year 2019 alone, with over 60 percent more drugs first coming to the market in the U.S. between 2010 and 2019, which underscores how effective private markets are in quickly adapting to patient needs. We ought to be finding out more about these opportunities and the innovation that they require, as well.

Further, the U.S. Food and Drug Administration, the Biomedical Advanced Research Development Authority, and Defense Advanced Research Projects Agency, DARPA, are all Federal entities working directly with our partnering—with industry leaders, developing cutting-edge technologies, and we want to know how ARPA-H will fit within these ongoing efforts within the private sector, and these agencies, and especially since there are still some unanswered questions of how the agency will function, and I think still where it will actually be housed.

So we are looking forward to working with members of this committee. We want to get answers to these questions about ARPA-H, and we—but we do want to work and find policies that will bring about innovations and cures that will help the lives of our fellow citizens. And we thank you so much.

[The prepared statement of Mr. Guthrie follows:]

PREPARED STATEMENT OF HON. BRETT GUTHRIE

Opening Statement of The Honorable Brett Guthrie
“ARPA-H: The Next Frontier of Biomedical Research”

February 8, 2021

As Prepared for Delivery

Thank you, Chair Eshoo for holding this hearing.

I first want to express how disappointed I was to hear about how the now former Director Lander – who until yesterday served in a cabinet level position for President Biden – disrespected and demeaned his staff at the White House. I am glad to hear that President Biden accepted his resignation, which is why he is unfortunately not with us today.

Today, we are discussing the proposal of creating the Advanced Research Projects Agency for Health (ARPA-H). This would establish a new DARPA-like agency housed within the National Institutes of Health.

Others and I on this committee have been strong supporters of health care innovation, specifically biopharmaceutical and biomedical research. A great success story is Operation Warp Speed, which was established by President Trump at the beginning of the COVID-19 pandemic.

In fact, there are many issues in health care we can and need to address on a bipartisan basis. However, President Biden is making it increasingly more difficult to support proposals like ARPA-H when he consistently promotes partisan legislation, like the Build Back Better Act, that would crush our biopharmaceutical innovation as we know it today.

Further, before moving forward with creating a new agency under NIH, I believe there are some significant scientific research integrity issues that have gone unchecked at NIH that need to be addressed before we allocate more federal resources toward publicly funded biomedical research.

Last Congress as Ranking Member of the Oversight and Investigations Subcommittee, I co-led a letter to Director Collins of NIH and Director Wray of the FBI to request information on how their agencies are working to remove foreign influence from biomedical research. NIH is the largest funder of

biomedical research in the world and Director Wray described how researchers from China can mask their identity to accept millions of U.S. grant dollars to steal U.S.-backed biomedical research to give China a competitive edge.

I also know some of my Republican colleagues on this committee have been actively leading on this issue and call on our Democratic colleagues to join us in this fight to protect this critical research.

To be clear, I believe these hearings are important to understanding the gaps in care across our health care system and how an agency like ARPA-H could close these gaps. I do have questions about if this agency would undermine research efforts being led by similar federal agencies in addition to our private sector partners.

ARPA-H is anticipated to be housed within the NIH whose mission is to conduct fundamental basic research to ensure we have a foundational understanding of how biological systems work. The private sector, not the NIH, is responsible for bringing breakthrough therapies to market, as only 5% of NIH funded research initiatives result in treatments that come to the market and only yield six new patents for every \$100 million spent on research.

The Congressional Budget Office data further shows that the pharmaceutical industry invested \$83 billion in research and development in fiscal year 2019 alone with over 60% more drugs first coming to market in the U.S. between 2010 and 2019, which underscores how effective private markets are in quickly adapting to patient needs. We ought to be finding more opportunities to allow this critical innovation to thrive.

Further, the U.S. Food and Drug Administration (FDA), the Biomedical Advanced Research and Development Authority (BARDA), and DARPA are all federal entities working directly with or partnering with industry leaders developing cutting-edge technologies and patient therapies. I wonder how ARPA-H could impact our ongoing efforts within the private sector, and these agencies, and especially since there are still some unanswered questions about how the agency will function.

I look forward to working with members of this committee to getting some answers to my questions about ARPA-H and working to promote policies that will allow for more biomedical research to successfully reach patients. Doing so will be imperative to save more lives.

Mr. GUTHRIE. And Madam Chair, I will yield back.

Ms. ESHOO. Thank you. The gentleman yields back.

The Chair is now pleased to recognize the chairman of the full committee, Mr. Pallone, for your 5 minutes of—

Mr. PALLONE. Thank you.

Ms. ESHOO [continuing]. Or an opening statement.

OPENING STATEMENT OF HON. FRANK PALLONE, JR., A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY

Mr. PALLONE. Thank you, Chairwoman Eshoo. Today the committee will examine the Biden Administration's proposal to establish the Advanced Research Projects Agency for Health, or ARPA-H, and how this proposal could enhance the landscape of biomedical research.

There is a lot of excitement for ARPA-H. Patient groups, academia, industry, and many others have voiced their support of this novel model to catalyze society-changing medical breakthroughs. Imagine a world with cancer-curing vaccines, no overdose deaths, a genetic test to detect and actually prevent illness, and a truly equitable health delivery system. It is hard to imagine at this point with COVID, but the possibilities with ARPA-H are endless.

Today America's existing biomedical research ecosystem is the best in the world. It is supported by the best universities, companies, and scientists. But there are still gaps and missed opportunities. Fundamental research conducted by universities, non-profits, and government agency requires a high degree of scrutiny in order to produce strong and objective knowledge. Once fundamental knowledge is established, translational science within the commercial sector takes over to develop cures, treatments, and technologies that address patient needs.

And this process involves a degree of risk that often times stands in the way of making lifesaving discoveries. Some of the risk factors include cost and recruitment for clinical trials, scalability, regulatory pathways, and the question of profit. At the end of the day, the priorities of the academic and commercial sectors may result in ideas simply not being pursued that are considered too high-risk, having a significant cost, or where the potential commercial market would not support the cause.

So advanced research agencies like the Defense Advanced Research Projects Agency, or DARPA, have addressed these gaps. DARPA has done this by building on established fundamental research, and funding time-limited, milestone-based translational research. This high-risk, high-reward model allows the defense research ecosystem to understand what works and what does not, without spending decades of resources on trial and error. And as a result, DARPA has developed platform technologies that have changed the world, technologies that we use every day, including cell phones, the internet, flat screen displays, and global positioning systems.

DARPA is part of the Department of Defense and, importantly, it has not supplanted any function of the Department's vast structure because its mission is unique and specific. So the same is true for ARPA-H. Its mission is to make pivotal investments in break-

through technologies that can't readily be accomplished through traditional research and commercial activity. And I look forward to hearing from our panel of expert witnesses who have decades of experience in academia, fundamental research, Federal public health agencies, and, of course, DARPA to discuss the mission structure, authority, timing, and funding of ARPA-H.

Now, although this is not a legislative hearing, appropriators have introduced legislation that will fund ARPA-H at \$3 billion in the House and 2.4 billion in the Senate. And that funding is contingent on this subcommittee writing and passing authorizing legislation. There are two existing proposals that would do so, one introduced by Chairwoman Eshoo and the other introduced by Representative DeGette. And I want to thank both of them for their outstanding leadership on this important issue.

This subcommittee has a strong bipartisan history of supporting Federal biomedical research. The proposal for ARPA-H is another opportunity for us to work together and establish an agency that will have a direct impact on fundamental research, breakthrough technologies, and healthier patient outcomes, and, of course, keep us at the forefront of biomedical research in the United States.

[The prepared statement of Mr. Pallone follows:]

PREPARED STATEMENT OF HON. FRANK PALLONE JR.

Committee on Energy and Commerce

Opening Statement as Prepared for Delivery
Of
Chairman Frank Pallone, Jr.

Hearing on “ARPA-H: The Next Frontier of Biomedical Research”

February 8, 2022

Today the Committee will examine the Biden Administration’s proposal to establish the Advanced Research Projects Agency for Health or ARPA-H, and how this proposal could enhance the landscape of biomedical research.

There is a lot of excitement for ARPA-H. Patient groups, academia, industry, and many others have voiced their support of this novel model to catalyze society-changing medical breakthroughs.

Imagine a world with cancer-curing vaccines, no overdose deaths, genetic tests to detect and actually prevent illness, and a truly equitable health delivery system. It is hard to imagine at this point, but the possibilities with ARPA-H are endless.

Today, America’s existing biomedical research ecosystem is the best in the world. It is supported by the best universities, companies, and scientists.

But there are still gaps and missed opportunities. Fundamental research, conducted by universities, nonprofits and government agencies, requires a high degree of scrutiny in order to produce strong and objective knowledge. Once fundamental knowledge is established, translational science within the commercial sector takes over to develop cures, treatments, and technologies that address patient needs.

This process involves a degree of risk that oftentimes stands in the way of making lifesaving discoveries. Some of the risk factors include cost and recruitment for clinical trials, scalability, regulatory pathways, and the question of profit. At the end of the day, the priorities of the academic and commercial sectors may result in ideas simply not being pursued that are considered too high-risk, have a significant cost, or where the potential commercial market would not support the cost.

Advanced research agencies like the Defense Advanced Research Projects Agency or DARPA have addressed these gaps. DARPA has done this by building on established fundamental research and funding time-limited, milestone-based translational research. This high-risk, high-reward model allows the defense research ecosystem to understand what works and what does not without spending decades of resources on trial and error.

As a result, DARPA has developed platform technologies that have changed the world – technologies that we use every day, including cell phones, the internet, flat-screen displays, and

February 8, 2022

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Global Positioning Systems. DARPA is part of the Department of Defense, and importantly it, has not supplanted any function of the Department's vast structure because its mission is unique and specific.

The same is true for ARPA-H. Its mission is to make pivotal investments in breakthrough technologies that cannot readily be accomplished through traditional research and commercial activity. I look forward to hearing from our panel of expert witnesses who have decades of experience in academia, fundamental research, federal public health agencies, and DARPA to discuss the mission, structure, authority, timing, and funding of ARPA-H.

Although this is not a legislative hearing, appropriators have introduced legislation that would fund ARPA-H at \$3 billion in the House and \$2.4 billion in the Senate. That funding is contingent on this Subcommittee writing and passing authorizing legislation. There are two existing proposals that would do so, one introduced by Chairwoman Eshoo and the other introduced by Representative DeGette. I thank you both for your outstanding leadership on this important issue.

This Subcommittee has a strong, bipartisan history of supporting federal biomedical research. The proposal for ARPA-H is another opportunity for us to work together and establish an agency that will have a direct impact on fundamental research, breakthrough technologies, and healthier patient outcomes.

Thank you.

Mr. PALLONE. So I thank you again, Chairwoman Eshoo, and I yield back the balance of my time.

Ms. ESHOO. The gentleman yields back. And now the Chair now recognizes the ranking member of the full committee, Representative Cathy McMorris Rodgers.

**OPENING STATEMENT OF HON. CATHY McMORRIS RODGERS,
A REPRESENTATIVE IN CONGRESS FROM THE STATE OF
WASHINGTON**

Mrs. RODGERS. Thank you, Madam Chair. I too want to associate myself with your comments regarding Dr. Lander. The question before this committee this morning is whether to create a new agency, ARPA-H, partly driven by the growing concerns as to the culture at NIH. Given Dr. Lander's sudden resignation last night, it only raises more questions in my mind as to what is really going on at NIH, and the culture at NIH.

I too want to thank the second panel for their flexibility in being—appearing before this committee earlier than you first anticipated.

We are discussing the proposal to address and create the Advanced Research Agency for Health, ARPA-H. It is a new biomedical research agency with the initial price tag of 6.5 billion over three years.

We are all proud that the United States is the leading nation leading the world in biomedical research and innovation. Still, millions continue to suffer from diseases that do not have any treatment. I have been a long-time supporter of NIH. I have supported doubling the funding at NIH. I have supported projects like the Brain Initiative, intended to speed scientific research necessary to accelerate cures for neurologic diseases. But I do have some concerns with this particular proposal, and I want to address it in three main areas.

Its intent ignores actions by the Biden Administration and Speaker Pelosi that will destroy medical innovation, such as the government price controls.

NIH is not cooperating or being transparent with Congress on how existing research funded by taxpayer dollars is being spent, especially in China.

And last, many questions about the ARPA-H proposal itself remain unanswered.

Regarding innovation, my colleagues and I will send a letter to Secretary Becerra today to detail how the proposed national coverage determination for all biologics targeting amyloid for Alzheimer's will devastate innovation, and hurt patients who rely on it. Bipartisan members of this committee have also written in opposition to the Administration's decision to repeal a final rule that would have provided Medicare coverage for FDA-approved breakthrough medical devices.

I am concerned that innovation-crushing decisions like these are a preview of how the Administration would abuse its power under government price controls. If innovation is truly what ARPA-H is about, re-proposing the NCD for Alzheimer's patients and innovators, giving them hope, reinstating the innovative medical

device regulations, and abandoning government price controls are reasonable steps we should all take.

Second, I am not convinced that a brand new agency is the answer to or will be able to overcome the institutional, cultural, and bureaucratic barriers that are present at our Federal scientific agencies. Our COVID-19 origins investigation has revealed that NIH has failed to do proper oversight and ensure accountability over research dollars, especially the risky research in China. Right now NIH has a long way to go to build trust. It should start by providing complete transparency by complying with congressional oversight.

Before we give the executive branch more authority and resources, let's make sure that we get the answers on what is being spent today, and why.

Onto ARPA-H itself. There is a fundamental question about the role of the private sector and the role of the Federal Government. Right now ARPA-H seems to lack a clear mission. I have asked for clarity from passionate advocates, researchers, the Biden Administration, Dr. Collins. I asked Dr. Lander the last time we spoke. Everyone has a different answer. How can we hold an agency accountable for success without clear, measurable goals?

I am concerned about duplication. In 2006 the NIH launched the Common Fund Program using a venture capital framework to tackle high-risk, milestone-driven projects to remove roadblocks in medical research that impede basic scientific discovery. In 2021 the program received over \$640 million. In 2011 a new NIH center for biomedical science, NCATS, was established to "catalyze a generation of innovative methods and technologies."

In the 21st Century Cures Act Congress established the Cures Acceleration Network to reduce significant barriers between research, discovery, and clinical trials. 21st Century Cures gave NIH other tools to advance biomedical research, such as funding opportunities for young investigators, a specific program called High-Risk, High-Reward Research, and funded the Cancer Moonshot and the Brain Initiative, the Regenerative Medicine Innovation Project, and the All of US research program. Are these existing programs not working?

Let's do the oversight. A new agency brings a lot of other costs.

Again, I am totally supportive. I want America to lead in innovation and medical research, but let's make sure that we are doing the job we need to do, this committee oversight of existing programs.

[The prepared statement of Mrs. Rodgers follows:]

PREPARED STATEMENT OF HON. CATHY McMORRIS RODGERS

Cathy McMorris Rodgers
House Energy and Commerce Committee
Subcommittee on Health
“ARPA-H: The Next Frontier of Biomedical Research”
February 8, 2022
As Prepared for Delivery

Thank you, Madam Chair.

Demeaning and embarrassing subordinates--in particular, women-- is inexcusable.

What was reported yesterday about OSTP's toxic workplace culture certainly raised questions we planned to ask Dr. Lander today about President Biden's zero tolerance policy for political appointees.

Dr. Lander resigned last night. It's curious what transpired between yesterday's White House press briefing and 9PM

We were informed around the same time of his resignation, the administration would not send anyone today to discuss the President's priority, ARPA-H, with the authorizing committee.

I want to thank the second panel for their flexibility in being available earlier than we anticipated.

Today, we are discussing the Biden administration proposal to create the Advanced Research Agency for Health, or ARPA-H, a new biomedical research agency with an initial price-tag of \$6.5 billion over 3 years.

The United States is leading the world in biomedical research and innovation.

Still, millions continue to suffer from diseases that do not have any treatment.

I have been a long-time supporter of NIH and projects like the BRAIN Initiative, intended to speed scientific research necessary to accelerate cures for neurologic diseases.

But I have concerns with this new agency for three main reasons:

Its intent ignores actions taken by the Biden-Harris administration and Speaker Pelosi that will destroy medical innovation, such as their push for socialist price controls.

NIH is not cooperating or being transparent with Congress on how existing research funded by taxpayer dollars is being spent... particularly in China.

And lastly, many questions about the ARPA-H proposal itself remain unanswered.

Democrat Anti-Innovation Proposals

Regarding innovation....

My colleagues and I will send a letter to Secretary Becerra today to detail how the proposed national coverage determination for **all** biologics targeting amyloid for Alzheimer's will devastate innovation and hurt patients who rely on it.

Bipartisan members of this Committee have also written in opposition to the Administration's decision to repeal a final rule that would have provided Medicare coverage for FDA-approved breakthrough medical devices.

I'm concerned that innovation-crushing decision likes these is a preview of how the Biden administration would abuse its power under socialist price controls.

If innovation is truly what ARPA-H is about...

.... re-proposing the NCD for Alzheimer's patients and innovators, reinstating the innovative medical device regulations, and abandoning price controls are all reasonable steps we should take first.

Lack of Accountability

Second, I'm not convinced that a brand-new agency is the answer to, or will be able to overcome, the institutional, cultural, and bureaucratic barriers that are present at our federal scientific agencies.

Our COVID-19 origins investigation has revealed the NIH has failed to do proper oversight and ensure accountability over research dollars, particularly for risky research in China.

Right now, NIH has a long way to go to build trust. It should start by providing complete transparency by complying with congressional oversight.

Before we give the executive branch more authority and resources, let's make sure we can get answers on what's being spent today and why.

ARPA-H Specific Concerns

On to ARPA-H itself, there is a fundamental question about the role of the private sector and the role of the federal government.

ARPA-H seems to lack a clear mission.

I've asked for clarity from passionate advocates, researchers, the Biden administration, Dr. Collins, and I asked Dr. Lander when we spoke.

Everyone has a different answer.

How could we hold an agency accountable for success without clear measurable goals?

Lastly, I'm concerned about duplication.

In 2006, the NIH launched the Common Fund program, using a venture capital framework to tackle high-risk, milestone-driven projects to remove 'roadblocks in biomedical research that impede basic scientific discovery.'

In 2021, this program received over 640 million dollars.

In 2011, a new NIH center for biomedical science, NCATS (*N-CATS*), was established to quote 'catalyze the generation of innovative methods and technologies.'

In the 21st Century Cures Act, Congress established the “Cures Acceleration Network” to reduce significant barriers between research discovery and clinical trials.

21st Century Cures gave the NIH other tools to advance biomedical research, such as funding opportunities for young investigators, a specific program for “High Risk, High Reward” research, and funded the Cancer Moonshot, the BRAIN Initiative, the Regenerative Medicine Innovation Project, and the All of Us Research Program.

Are these existing programs not working? Let’s do oversight to learn if they can be leveraged better.

A new agency seems like an extreme solution, bringing with it new administrative staff, IT, and other overhead dollars that won’t go to research.

Closing

Again, America has led the world in innovation and medical research. I want to keep it here and do all I can to further unleash it.

ARPA-H, like the America COMPETES Act and other well-intentioned ideas, put more money into a system before doing the necessary homework on what exactly the problem is and what programs we already have that could be helping, or slowing, that innovation.

I yield back.

Mrs. RODGERS. I yield back. Thank you.

Ms. ESHOO. The gentlewoman yields back.

The Chair would like to remind Members that, pursuant to committee rules, all Members' written opening statements will be made part of the record.

Now this is one of the best parts of the hearing, is to introduce our witnesses. And we—colleagues, this is really a sterling panel of witnesses.

The first, Dr. Keith Yamamoto, and he is here with us in person. He is the vice chancellor for science policy and strategy, director of precision medicine, and professor of cellular and molecular pharmacology at the University of California, San Francisco.

Welcome to you, Dr. Yamamoto. It is an honor to have you with us.

Virtually we have Dr. Esther Krofah. She is the executive director of FasterCures and the Center for Public Health at the Milken Institute.

Thank you to you for being with us.

Dr. Geoffrey Ling, here in person, is the CEO of On Demand Pharmaceuticals, a Johns Hopkins School of Medicine professor, and Johns Hopkins Hospital attending physician. Dr. Ling also served as the founding director of DARPA's biological technologies office, and is a retired colonel with 21 years of service as an Army medical officer.

It really is difficult to abbreviate your backgrounds. So, colleagues, I am just giving a snapshot. But if you go into the testimony and the bios, you will be reading, single space, for quite a while. Our country is blessed with the leadership of each one of these individuals.

Dr. Brett Giroir has served as the assistant secretary of health at HHS. He has testified many times at our committee, the acting FDA commissioner, director of the defense sciences office at DARPA, and admiral in the U.S. Public Health Service Commissioned Corps.

Welcome to you, Dr. Giroir. It is good to have you with us once again.

Dr. Brian Miller is here with us in person. He is a practicing hospitalist, and an assistant professor of medicine and business at the Johns Hopkins University School of Medicine.

Welcome to you.

So to each one of you, we are proud to have you here. We are grateful to you. We look forward to your testimony.

For those that are here with us in person, you are probably familiar with the system of lights here in front of you. You have 1-minute remaining when the light turns yellow, and I think everyone knows what a red light is signaling.

So, Dr. Yamamoto, thank you again. You have 5 minutes for your testimony.

STATEMENT OF KEITH R. YAMAMOTO, PH.D., VICE CHANCELLOR FOR SCIENCE POLICY AND STRATEGY, UNIVERSITY OF CALIFORNIA SAN FRANCISCO; ESTHER KROFAH, EXECUTIVE DIRECTOR, FASTERCURES AND CENTER FOR PUBLIC HEALTH AT THE MILKEN INSTITUTE; GEOFFREY SHIU FEI LING, M.D., PH.D., CEO, ON DEMAND PHARMACEUTICALS PROFESSOR OF NEUROLOGY, JOHNS HOPKINS MEDICINE; BRETT P. GIROIR, M.D., ADMIRAL, FORMER ASSISTANT SECRETARY FOR HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; AND BRIAN JAMES MILLER, M.D., M.B.A., M.P.H., PROFESSOR OF MEDICINE, JOHN HOPKINS MEDICINE

STATEMENT OF KEITH R. YAMAMOTO, Ph.D.

Dr. YAMAMOTO. Good morning, Chairman Eshoo, Ranking Member Guthrie, and members of the subcommittee. It is also nice to see my friend, Congressman DeGette, here, as well. And it is an honor to present a statement before you today.

I shall address two questions: first, why at this moment of spectacular discoveries about biological mechanisms and disease, most of them NIH-sponsored, should Congress be establishing another agency, ARPA-H; and second, why should Congress ensure that ARPA-H is fully independent, with a culture and practices that seem almost polar opposites to NIH's successful model?

First, why ARPA-H now? The policy framework for Federal support of U.S. science and technology was set in 1945 by President Roosevelt's science adviser. Government would fund basic research—that is, discovery of new knowledge—and training of future generations of scientists. Industry would then develop the new knowledge into products from which they would profit, and the American people would enjoy a happier, more secure quality of life.

In the case of health, for example, we needed basic research to understand biological processes, how molecules collaborate to make cells, tissues, organs, and healthy human beings. Basic research has to be untargeted. We don't know what we don't know. So NIH created a competitive funding program giving university scientists freedom to let their curiosity, ingenuity, and expertise determine which biological processes they wish to study, and how they would study them.

NIH's funding apparatus is driven by peer review. Working scientists serve on committees to decide which proposals submitted by their colleagues will win funding. With many scientists each pursuing whichever biological process intrigues them, the gaps in our knowledge are being filled.

Now, peer review is not perfect. Dr. Francis Collins, just retired as NIH director, acknowledged that the NIH process "is a little slow, a little conservative, not necessarily going to embrace the transformative projects." Yet this curiosity-driven model is, by any measure, the world's greatest knowledge discovery engine for biomedical research. For example, 99 of the 230 Nobel Prizes ever awarded in chemistry, physiology, or medicine have gone to 163 NIH-supported scientists. Astonishing dominance.

However, new knowledge alone is insufficient to motivate industry to develop applications. Among the 9,000 known human diseases, there are approved treatments for only about 500. And among the 24 most impactful drugs on the market, the median time between the key bit of knowledge discovery and FDA approval was 32 years.

Clearly, biotechs face many barriers: economic risk too high, near-term markets too small, scope too broad for any one company to realize profit, industry alone unable to do the job. Thus, Federal science and technology policy needs a revise. Government support is required to de-risk industry participation, and government coordination and management are required to set and meet audacious goals. That is ARPA-H.

So question No. 2, why should Congress endow ARPA-H with a drastically different culture and operating model? Consider first ARPA-H's distinctive goals. Its starting point is NIH's endpoint: discovered knowledge is the foundation for ARPA-H development of platform technologies, devices, therapeutics. It seeks applications, rather than discovery of knowledge to demonstrate feasibility of transformative concepts, de-risking development.

Next, look at the ARPA-H operating model, which draws on DoD's DARPA, which Drs. Ling and Giroir will discuss, and may have been mentioned here already. Support and manage program-specific, transdisciplinary, multi-sector partnerships and teams to meet contract goals set in and enforced by ARPA-H program managers. Embrace bold approaches, tolerate failure, create advanced technologies, computational tools, novel materials, imaging methods all leveraged on chronic and infectious diseases, and on countless rare diseases which afflict millions, but receive scant attention due largely to market size concerns.

None of this looks like NIH, so ARPA-H needs to look and act differently. At the same time, though, NIH must continue to thrive for ARPA-H to succeed. Thus, Congress should install safeguards to prevent ARPA-H funding from supplanting NIH investments or threatening its culture.

For ARPA-H itself, Congress should provide independence to construct a flat, nimble operating model that supports program managers, each overseeing a daunting health challenge and a bold path to its solution. Congress should grant the director and program managers authorities, flexibilities, and, yes, appropriations for hiring, diversity, contracting, broad partnering, and ethical and efficient IP and tech transfer.

Importantly, ARPA-H should be authorized as an independent agency within HHS, rather than as a component of NIH. Dr. Regina Dugan, a renowned former director of DARPA, puts it this way: "An organization like the ARPA-H exists to challenge conventional wisdom. Don't put it inside the very organization that holds the conventional wisdom." Creating a new culture and operating model is always difficult, but creating it within a very different and long-established one is likely impossible.

Thus, the actions of Congress in authorizing these agencies will influence, if not determine, its success or failure. Thankfully, the legislation developed by Chairwoman Eshoo and all of you wisely

recognizes the critical elements of independence, authority, culture, policy, and practice that will place ARPA-H on a positive trajectory.

ARPA-H repairs a weakness in our Federal science and technology policy. ARPA-H will consolidate new scientific knowledge and devise strategies and tools that improve and extend lives for all, including those long disadvantaged.

This concludes my testimony. I would be pleased to answer any questions. Thank you again for the opportunity to?

[The prepared statement of Dr. Yamamoto follows:]

ARPA-H: The Next Frontier of Biomedical Research

Statement of Keith R. Yamamoto, PhD 

Vice Chancellor, Science Policy and Strategy

Director, UCSF Precision Medicine

Professor Emeritus, Cellular and Molecular Pharmacology

University of California, San Francisco

Before the

Subcommittee on Health

Committee on Energy and Commerce

U.S. House of Representatives

February 8, 2022

Good morning, Chairwoman Eshoo, Ranking Member Guthrie and Members of the Subcommittee. Thank you for the honor of your invitation to present a statement before you today.

I am Keith R. Yamamoto PhD, Vice Chancellor for Science Policy and Strategy, Director of Precision Medicine and Professor of Cellular and Molecular Pharmacology at the University of California, San Francisco. I received a Bachelor of Science from Iowa State University and a PhD from Princeton University before migrating to San Francisco, where I have been on the faculty for 45 years. My molecular biology lab, which I recently closed, studied the detailed mechanisms by which small molecules made in our bodies, hormones, control important physiological processes such as metabolism, stress responses and immunity; that research has been recognized by my election to the National Academy of Sciences, the National Academy of Medicine and the American Academy of Arts and Sciences, and Fellowship in the American Association for the Advancement of Science, among other honors. In the course of that work, I had the privilege, pleasure and primary responsibility for mentoring approximately 100 PhD students and postdoctoral scholars. Our research was funded throughout by grants from NIH and NSF, as well as grants and fellowships from private foundations.

For my entire career, I have also been active in matters of science and public policy, leading or serving on dozens of committees focused on a broad range of issues, challenges and opportunities, including chairing or participating in 28 NIH advisory

councils, working groups, special initiatives, task forces and review panels focused on the operating principles and practices of that agency, and the investigator-focused culture that grounds every element of its function. I enjoyed the opportunity to interact with, and consult informally, with Dr. Geoffrey Ling, while he developed and directed the DARPA Biotechnology Office under an operating model very different from that at NIH. I also chaired the Board on Life Sciences for the National Academy of Sciences, which produced during that time two relevant reports, “A New Biology for the 21st Century” and “Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease”; co-chaired a study committee for the American Academy of Arts and Sciences that authored a report, “Unleashing America’s Research and Innovation Enterprise”; and currently co-chair the Science & Technology Action Committee, which is advocating for specific ways that federally supported science and technology can contribute bold solutions to existential societal challenges, including those in public health and healthcare.

These and other activities have provided me with a perspective on two related questions that I’ll address today: [1] why, at this moment of spectacular fundamental discoveries about biological mechanisms and disease, most of them sponsored by NIH, should Congress establish yet another agency, ARPA-H; and [2] why should Congress act assertively to ensure that ARPA-H is fully independent, with authority to establish a culture, operating principles and practices that at first glance appear almost polar opposite to NIH’s successful model? The answers to these two questions, in my view,

justify the title of this hearing, ARPA-H, the Next Frontier of Biomedical Research.

US science policy: fund university-based knowledge discovery and training

“Without scientific progress the national health would deteriorate; without scientific progress we could not hope for improvement in our standard of living or for an increased number of jobs for our citizens; and without scientific progress we could not have maintained our liberties against tyranny.” So wrote Vannevar Bush, President Roosevelt’s science advisor in 1945, in a pivotal report that set the framework for federal support of US science and technology. That policy directed government funding into *basic* research, the discovery of new knowledge that “provides scientific capital”, as well as training future generations of scientists. Industry, the report asserted, would then take over, innovating and developing the newly discovered knowledge into products from which they, and the American people, would profit. The companies would make money, and the people would enjoy a healthier, happier, more secure, quality of life.

In order to prevent, treat and cure diseases, for example, we needed first to understand more about biological processes – how molecules collaborate to make cells work, how cells specialize to form tissues, organs, organ systems, and how those systems interact to produce a healthy human being. And, what goes wrong in disease

Because we knew so little in 1945, *basic* research would be untargeted – we didn't know what we didn't know. And still today, there's vastly more unknown than known. So, the NIH strategy was to create a competitive funding program for university-based scientists and their trainees, giving scientists complete freedom to choose which biological process they wished to study, and to use their expertise and ingenuity to define their experimental approach, biological system, etc.

NIH set up a unique-in-the-world funding apparatus driven by peer review, in which working scientists volunteer to serve on committees that judge the merits of research proposals submitted by their colleagues, with those peer evaluations determining which would win funding needed to carry out the work. In this system, success is defined as new knowledge uncovered – and because not every idea is right and not every approach works, NIH funded research projects often deviate from proposed plans. Not infrequently, however, serendipitous observations take scientists down unanticipated paths to new knowledge, perhaps in an entirely different area of biology -- but new knowledge nonetheless. With enough trained scientists, each supported by NIH to pursue whatever biological process intrigues them, the gaps in our knowledge are being filled to create a progressively detailed picture of how biology works, and how it can go wrong.

This untargeted, peer review system is not perfect. First, those reviewers in their day jobs are the very scientists whose work has defined the prevailing paradigms – the

consensus opinions on how things work. So, they tend not to be supportive of bold ideas that challenge the conventional thinking. Second, working scientists tend to review favorably proposed experiments that seem the most likely to succeed, so risky studies, those taking on a big challenge or trying out an untested idea, are deprioritized relative to those that take small incremental steps. Finally, NIH-funded research projects advance slowly, with unexpected findings not infrequently diverting scientists into areas different from those proposed. Dr. Francis Collins, just retired after twelve years as Director of NIH, has acknowledged that the NIH process “is a little slow, maybe a little conservative, and it isn't necessarily going to embrace the really big transformative projects.”

Yet, despite its weaknesses, the NIH culture and operating model -- curiosity-driven, individual scientist-driven – is by any measure, the world's greatest knowledge discovery engine for biomedical research. Take the Nobel prizes, for example: three are awarded each year for fundamental scientific discoveries, considering scientists the world over – of the 230 Nobel prizes in chemistry, physiology or medicine that have been awarded, 99 have gone to 163 NIH-supported scientists. Astonishing dominance. The NIH knowledge discovery model works!

Federal support is needed for breakthrough applications of new knowledge

At first glance, it appears that our federal science policy has got it right – funding knowledge discovery seems sufficient to motivate private sector development of applications that serve society. For example, of the 210 new drugs approved by FDA between 2010 and 2016, pharma-driven development of every single one of them originated from new knowledge uncovered by NIH-funded research. However, the process is painfully, alarmingly slow. Among the 24 most impactful drugs on the market (as judged by a physician survey), the median time between the key bit of knowledge discovery and FDA approval was 32 years!

Moreover, severe underinvestment relative to potential impact leaves many ideas simply unpursued. Among the 9000 known human diseases, there are approved treatments for only about 500. Pharma and biotechs face many barriers: (i) perceived risk in the hypercompetitive global economy is too high; (ii) the near-term market is considered too small; (iii) the scope is so broad that no single company can capitalize on an opportunity and expect to realize economic benefit; (iv) successful development would require coordination across multiple sectors – industry, government, universities – to bring together the needed skills and resources.

Thus, federal science and technology policy must adapt to a new reality: profit motive is *not* sufficient for industry to fully fund the bold innovation and development needed to rapidly create applications of new knowledge that serve the public. Moreover, industry alone cannot and should not “go it alone” with these challenges. Government

support is required to de-risk industry participation, and government coordination and management is required to create multisector partnerships and teams capable of setting and meeting audacious milestone driven goals. Clearly, NIH's curiosity-driven, individual scientist-dependent, serendipity-redirected, peer review-governed culture and process, remarkably powerful as a knowledge discovery engine, won't suffice.

ARPA-H: Transformative Application of New Knowledge to Counter Disease

ARPA-H promises a culture and operating model very different from NIH. Its goals, strategies and outputs would not overlap or duplicate NIH efforts, but rather exploit NIH-discovered knowledge as a foundation for innovative development of breakthrough platform technologies, devices, therapeutics, diagnostics and preventatives. ARPA-H will deliver transformative advancements in health by building program-specific, transdisciplinary, multi-sector partnerships and teams -- de-risking industry participation in particular.

The teams will be assembled to achieve tightly-focused contract goals set and maintained by ARPA-H program managers, who themselves are in term-limited positions "on loan" from industry, government and academia, bringing urgency to the execution and completion of their stated goals. The teams will establish unique capabilities for developing and leveraging advanced technologies, powerful computational tools, novel

materials, revolutionary imaging methodologies and the like. Importantly, these efforts will be targeted to chronic and infectious diseases that sicken or kill hundreds of millions of people worldwide, and to countless rare diseases, which in aggregate, afflict many millions as well, but have not received needed and deserved attention, due in large measure to concerns over market-size. To be clear, the ARPA-H model will de-risk industry participation in development of treatments and cure of rare diseases.

For ARPA-H to succeed, Congress should provide both authorities and flexibilities that empower an ambitious, visionary director to construct a flat and nimble organization dependent on outstanding program managers, who themselves compete for and win appointment to the agency by defining an important but daunting health challenge, and a distinctive path to a breakthrough solution. Congress should ensure that the director and program managers are granted authorities for hiring diversity, contracting, cross-agency, cross-sector partnering, and ethical and efficient IP and tech transfer, and are appropriated sufficient funding to support their programs. Properly structured, these provisions will attract and resource powerful cross-sector teams willing to embrace bold, risky approaches, and willing to chance failure, in order to achieve transformational breakthroughs in health and disease.

In creating ARPA-H, it is essential that Congress recognize that NIH must continue to thrive for ARPA-H to succeed. Thus, safeguards should be put in place that prevent ARPA-H funding from supplanting NIH investment.

Finally, Congress would be wise to recognize that ARPA-H's success will depend upon its creation of a structure, culture, operating model and practices that differ dramatically from NIH, enabling it to take and overcome risks, to achieve breakthrough *applications*, rather than *discovery*, of knowledge. Program managers will envision problems at a different scope and scale than individual investigators, will propose radical solutions, and will recruit and build multidisciplinary teams that perform on and achieve milestone-driven contracts – all of that foreign to NIH's knowledge discovery approach.

To develop such a distinct culture and approach to problem visioning and solving, ARPA-H should be authorized as a free-standing agency within HHS, rather than as a component of NIH. Dr. Regina Dugan, former director of DARPA and now CEO of Wellcome Leap in the UK, where she is bringing an ARPA-like model and culture to biomedical research and development initiatives, has a clear-eyed perspective on the matter: "An organization like ARPA-H exists to challenge conventional wisdom. You shouldn't put it inside the very organization that holds the conventional wisdom." Dr. Dugan's intent here was not to denigrate "conventional wisdom", but rather to underscore that creating a new culture and operating model is difficult, but that developing a new culture within an existing, very different and highly established one may be impossible.

Thus, the specific actions of Congress in authorizing this agency will strongly

influence, if not actually determine, its success or failure. While this is not a legislative hearing, and it is thus inappropriate to delve into the details of a particular bill, let me say simply that the still-evolving legislation (HR5585) developed by Chairwoman Eshoo and her subcommittee wisely recognizes and takes into account the critical elements of independence, authority, culture, policy and practice that will place ARPA-H on a positive trajectory.

Perspective

ARPA-H is a concept for innovation, development and application of scientific knowledge that seeks to address points of weakness in our federal science and technology policy that have emerged since its establishment three quarters of a century ago. ARPA-H will consolidate new scientific knowledge, and will adopt risky strategies and approaches that, if successful, have the potential to extend and improve lives for all, including those long disadvantaged. Success of ARPA-H will depend on creation of a culture and operating model that attracts, de-risks and empowers innovative teams drawn from industry, private foundations, academia and government.

This concludes my testimony. I would be pleased to answer your questions or address your comments. Thank you again for the opportunity to consider this important matter with you.

Ms. ESHOO. Thank you, Dr. Yamamoto. Next we will hear testimony from Ms. Esther Krofah.

You have 5 minutes for your testimony.

STATEMENT OF ESTHER KROFAH

Ms. KROFAH. Thank you, Chairwoman Eshoo, Ranking Member Guthrie, and members of the Subcommittee on Health, for the opportunity to provide input on the proposed Advanced Research Projects Agency for Health, ARPA-H. My name is Esther Krofah, and I am executive director of two centers of the Milken Institute: FasterCures and the Center for Public Health.

FasterCures is driven by a singular goal, to save lives, by speeding scientific advancements to all patients. We like to say our name is our mission. With an independent voice, FasterCures is working to build a system that is effective, efficient, and patient centered. During the pandemic we have witnessed the rapid development of effective COVID-19 vaccines in under a year, and development of therapeutics and diagnostics that demonstrate how critical scientific discovery translated into real products and interventions save lives. But many patients are asking, if it can be done for COVID-19, can it also be done for my disease condition?

This morning I speak to you as my father is fighting stage four cancer, hoping for some more time so that he can see his children and grandchildren achieve their dreams. ARPA-H holds the promise to work at the cutting edge of science to take risks and achieve breakthroughs that can improve lives like my father's, but countless others.

FasterCures has long supported NIH DARPA-like authorities and capabilities for more high-risk, solutions-oriented R&D. So we are gratified that this concept is being seriously considered at this time.

My comments today will be in the following areas: the structure of the proposed new agency, including its location, leadership, authorities, and funding; second, its activities, including priority setting and coordination with other agencies and sectors.

Some have questioned whether ARPA-H should be housed within NIH, as currently proposed. There is, of course, a more recent example of the DARPA model that has been stood up and can be looked to for lessons learned. And that is ARPA-E, which resides within the Department of Energy, but employs an operating model like DARPA's. We have seen with ARPA-E that an entity like this can exist within a larger Federal agency, and still foster a different culture and operating model with the right toolkit and key ingredients. As such, we do not see a reason ARPA-H could not be situated within NIH and still accomplish its mission, including advantages to having easy access to other NIH infrastructure, personnel, programs, and expertise.

We would like to emphasize that this new entity should not be considered as a substitute for the National Center for Advancing Translational Sciences, NCATS. NCATS has a broad remit to support the whole field and discipline of translational and clinical research. That needs to remain distinct and well-supported.

Who leads a new ARPA-H entity will be critical, especially as its first leader, and should be selected by their visionary capacity and ability to inspire and empower a new team, directing milestone-driven initiatives. ARPA-H will need to ensure expertise from the private sector is engaged, both internally and externally. It should ideally have a leader with experience outside academia, with a proven track record of success and managing through failures. It will need an external advisory body comprised of patient organizations, industry, academia, and other non-profits to inform the agency's priorities.

Representatives should also include those from under-served minority communities, defining problems that are most important to be solved.

DARPA's program managers are a critical asset, and should also be for ARPA-H. Ensuring key people are recruited for those positions is central to the culture necessary for the success of this effort. This is likely to require freedom from the usual constraints of the Federal hiring process, in order to bring in the right people for limited durations, do it quickly, and pay them appropriately.

Perhaps more important than the exact budget number is a consistency of funding and sustainability over time. This needs to be a multi-year commitment of effort and funding. It is bigger than a 3-year budget line item.

Collaboration with other Federal agencies is necessary for the success of ARPA-H. FDA is, obviously, a critical link in the process that gets exciting new science and products into the hands of patients. We need to make sure they have the resources and expertise to keep pace and effectively regulate new technologies coming to them for review through efforts like ARPA-H.

There also needs to be active and regular engagement with other agencies critical to advancing solutions to patients, such as CMS and CDC.

ARPA-H should develop a data-driven and transparent process for setting priorities, including and prioritizing conditions with high unmet need and low innovation activity.

In creating this new entity, we should heed key lessons from the COVID-19 pandemic. Investment should be prioritized in platform technologies and research infrastructure.

I would like to conclude by thanking you for the opportunity to offer input. I am happy to discuss these ideas and answer any questions you may have.

[The prepared statement of Ms. Krofah follows:]

Written Testimony of

Esther Krofah

Executive Director of FasterCures and Center for Public Health, Milken Institute

Before the U.S. House Energy & Commerce Subcommittee on Health

“ARPA-H: The Next Frontier of Biomedical Research”

February 8, 2022

Thank you Chair Eshoo, Ranking Member Guthrie, and Members of the Subcommittee on Health for the opportunity to provide input on the proposed Advanced Research Projects Agency for Health (ARPA-H). My name is Esther Krofah, and I am Executive Director of two centers within the Milken Institute, FasterCures and the Center for Public Health.

FasterCures is driven by a singular goal: to save lives by speeding scientific advancements to all patients. With an independent voice, FasterCures is working to build a system that is effective, efficient, and driven by a clear vision: working with our partners to build a patient-centric system where science is accelerated, unnecessary barriers are overcome, and lifesaving and life-enhancing treatments get to those who need them as rapidly and as safely as possible.

FasterCures has long supported giving NIH DARPA-like authorities and capabilities for more high-risk, solutions-oriented R&D, so we are gratified that this concept is being seriously considered at this time.

My comments today will be in the following areas:

- I. The structure of the proposed new agency, including its location, leadership, authorities, funding and;
- II. Its activities, including priority-setting and coordination with other agencies and sectors.

I. STRUCTURE

Location. Some have questioned whether ARPA-H should be housed within NIH, as currently proposed. There is, of course, a more recent example of the DARPA model that has been stood up and can be looked to for lessons learned, and that is ARPA-E (Energy), which resides within the Department of Energy but was meant to serve a purpose and employ an operating model like DARPA's. The experience of ARPA-E should be examined in detail (the [National Academies](#) has already done some of that work) and critical success factors identified. We have seen with ARPA-E that an entity like this can exist within a larger federal agency and still foster a different culture and operating model, with the right toolkit and key ingredients. As such, we do not believe this is as critical a threshold question as others might.

We would like to emphasize that this new entity should not be considered a substitute for the National Center for Advancing Translational Sciences (NCATS) at NIH. Some projects of a type

currently pursued by NCATS might fit under the umbrella of ARPA-H, such as platforms like the Tissue Chip or 3-D Tissue Bioprinting programs. But NCATS has such a broad remit to support the whole field and discipline of translational and clinical research that it needs to remain a distinct and well-supported entity.

Leadership. Who leads a new ARPA-H entity will be critical, especially as its first leader, and should be selected for their visionary capacity and their ability to inspire and empower a new team directing milestone-driven initiatives.

ARPA-H will need to ensure expertise from the private sector is engaged both internally and externally. It should ideally have a leader with experience outside academia with a proven track record of success and managing through failures. It will need an external advisory body comprised of patient organizations, industry, academia, and other nonprofits, etc., to inform the agency's priorities.

DARPA's program managers are also a critical asset, and ensuring key people are recruited for those positions is central to the culture change necessary for the success of this effort. This is likely to require freedom from some of the usual constraints of the federal hiring process in order to bring in the right people for limited durations, do it quickly, and pay them appropriately.

Authorities. FasterCures advocated many years ago that NIH be given "Other Transaction Authority (OTA)," like DARPA and other agencies have, to allow for more rapid and flexible engagement with industry and academia to advance projects. NIH does have OTA now, and it is currently being utilized occasionally in NIH initiatives such as Stimulating Peripheral Activity to Relieve Conditions, or SPARC. This is the kind of important tool that will be central to ARPA-H's success.

Funding. Perhaps as or more important than the exact budget number is consistency of funding and sustainability over time. This needs to be a multi-year commitment of effort and funding; it is bigger than a three-year budget line item. A lack of consistent and stable funding for BARDA is arguably one reason the country was not as prepared for the onslaught of COVID-19 as we would have liked to be.

An important reminder for policymakers is that the entire budget of the Food and Drug Administration (FDA) is approximately \$6.5 billion. FDA is obviously a critical link in the process that gets exciting new science and products into the hands of patients, and we need to make sure they also have the resources and expertise to keep pace and effectively regulate new technologies coming to them for review through efforts like ARPA-H.

When NCATS was created, there was concern expressed that it would siphon funds away from the other NIH institutes and from basic scientific discovery; as we can see, the opposite has occurred, with significant growth in NIH's budget over the years.

II. ACTIVITIES

Priorities. ARPA-H should develop a data-driven and science-driven transparent process for setting priorities. For example, a recent HHS effort led by the Office of the Assistant Secretary for Health with the Agency for Healthcare Research and Quality (AHRQ) created a model to

prioritize conditions with high unmet need and low innovation activity in public health. We welcome such a strategic, consistent approach.

In creating this new entity, we should heed key lessons of the COVID-19 pandemic:

- Investment should be prioritized in platform technologies (e.g., mRNA, prototype pathogens) and research infrastructure (e.g., trial networks including community-based networks, data sharing/analytics platforms) that can benefit many researchers and developers.
- A number of high-value platforms and assets were created during the pandemic that should be sustained and made available to ARPA-H (e.g., RADx, the National COVID Cohort Collaborative data platform, NIH's Clinical Trial Capacity Inventory).
- Collaboration, across and within sectors, was key to accelerating research and product development during the pandemic.

Coordination and collaboration. A multi-agency and multi-stakeholder approach should be employed for setting priorities and guiding/informing projects. First, ARPA-H must ensure its work is complementary to and not duplicative of other science-funding agencies such as DARPA, NSF, and BARDA. Second, we strongly believe that representatives of patients, including those from underserved communities, must be a part of priority-setting, defining the problems most important to be solved. And finally, if ARPA-H's work is to be truly solutions-oriented, it must be actively and regularly engaged with and informed by other agencies critical to advancing solutions to patients such as FDA and CMS.

The private sector is a critical partner in this work, whether as collaborators in executing specific projects or as the recipients and amplifiers of any innovation coming out of the program. Technology transfer and commercialization will be central considerations in the policies and approach of the new agency.

Another aspect of working with the private sector could be finding ways to leverage private investment in technologies that might come out of ARPA-H. BARDA Ventures could be a potential model in this regard, or In-Q-Tel, which invests in new technologies related to national security.

Thank you again for the opportunity to offer our input. I am happy to discuss these ideas further and answer any questions you may have.

Ms. ESHOO. Thank you for your testimony.

Next, the Chair recognizes and thanks Dr. Geoffrey Ling for being with us today in person.

You have to know that this is some—it is a treat for us to have people here in person. It has been a rarity now for two years. So welcome to you, and you have 5 minutes for your testimony, Doctor.

STATEMENT OF GEOFFREY SHIU FEI LING, M.D., Ph.D.

Dr. LING. Thank you, Chairwoman Eshoo. Good morning, Ranking Member Guthrie and distinguished Members of the Congress. I have to tell you that—you have been thanking us, but I have to thank you. This is a life memory for me. So thank you all.

My name is Geoffrey Ling, and I want to start by saying I am an Army officer. So the way I talk, please forgive me, because I spent 21 years as a military officer. I served in the United States Army. I served in Afghanistan. I served in Iraq as a military physician.

I was fortunate, since leaving government service, to be able to go ahead and become CEO of my own company called On Demand Pharmaceuticals. I am also a professor of neurology at the Johns Hopkins, where I still practice medicine on occasion. I am getting kind of old for it, but it is what it is. So my comments are my own, please. They do not reflect that of Hopkins, On Demand, or U.S. Army.

Relevant to this hearing, I was the founding director of the biological technologies office at DARPA, and I served at the agency for 11 years. Also relevant to this hearing, I served for the NIH for 14 years. I was on advisory councils and study sections. So from this perspective, I am going to address my comments.

DARPA was found in 1958 in response to an existential threat: Sputnik. ARPA-H is being considered in the shadow of a real threat, COVID.

But in adversity, there is opportunity, there is a real chance to do something new, do something special, do something bold, and that is create an agency that says yes. Everybody else looks to say no. No is the easiest answer. It means you don't have to do anything, it means you are happy with the status quo. It means that you are just fine to go back to do what you were doing.

But you want an agency that says yes, yes, I will go after autism; yes, I will go after Alzheimer's; yes, I will go after glioblastoma multiforme, a brain tumor. And it is just not saying yes, it is knowing how to say yes. It is not about more money, it is about how to spend the money. Not what to spend the money on, but how to spend the money on.

When I was at DARPA we recognized that this is taxpayer money, not my money. This is not the investigator's money, it is taxpayer money, the people work every doggone day who expect you to perform against it to deliver something for them. And how do you do that? You do that by making sure that everybody knows what they are trying to accomplish.

This is about affirming, changing, or rejecting current clinical care. If you are not doing one of those three things, you are not doing the job. You want to affirm it, you want to reject it, you want

to change it. You have got to come to work every day, knowing that. You have got to come to work thinking that you have autism, or your child has autism. When we looked at DARPA performers, we expect them to have that level of commitment.

And what was given in return? DARPA program managers—ARPA program managers will work with those groups from end to end. It is not about doing the science. That is the first step. You have got to get through regulatory. Then someone has got to make it, then somebody has got to distribute it. And then the patient community has to embrace it. It is an end-to-end solution. Programs are meant to address all of these.

At the start of a DARPA BTO project, it is not just the scientists. It is the scientist who has been reviewed by, not peers, I am sorry, but they are reviewed by NIH officers, DoD science officers, FDA science officers. Why the FDA, you would ask? Because the FDA should be there at the beginning, because you got to get through them. It is a fact of life. If they are not there at the beginning, they are not going to be there at the end.

You have to resource these performers, give them the people they need, give them the equipment they need, give them the money they need. But do not give them the time they ask for. Time is the worst enemy we have. ARPA-H is going to be like DARPA. Hold them to time. You are going to say—a lot of people are saying, “Oh, I need more time, I need more time.” Those are not the people you want. You want the person who says, “Put me in, Coach. Put me in,” and recognize that it is not a gift. It is taxpayer money. If they are not delivering, fire them, get somebody else.

If you look at national baseball teams, who makes it to the World Series? It is the people who recognize that the inside infielder may not be the one you started with, may not be the one you are going to end with, because at the end of the day you are trying to get into the World Series. It is not about who, it is about the what. It is about the mission. Get the mission done.

So when I—when you ask, should there—an ARPA-H exist, of course. I am not going to go through all of the wonderful things that all of my friends have said. I agree with them completely. This is about how it should be constructed.

It should be independent. It needs to be independent, because you need people there who are going to have the determination, have the drive, have the urgency to get the job done, end to end. And it means, at the very outset, the scientists, the regulators, industry, and the patient advocacy groups, and the clinicians. If you don’t have them all there at the beginning, and you don’t have them throughout this, you will have the valley of death the Congresswoman—Chairwoman Eshoo, you are right.

We cross that by bridging it at the beginning. Look at how DARPA does this. The model exists. You are not looking for another model. It exists. All the authorities needed have been—already been awarded by the Congress. Just institute them in this agency of ARPA-H.

We talk about U.S. losing ground. Let me tell you right now, U.S. will not lose ground. I tell you why that is. Because of this. No totalitarian government would ever set up a DARPA, ever. Put smart people, fund them, turn them loose? Who in heaven’s name would

do that, if you were a totalitarian dictator? You wouldn't. You would only do it in our kind of environment.

So at the end of the day, I want to thank the committee for allowing me to speak. But I say that now is the time, and make it—please make it independent.

[The prepared statement of Dr. Ling follows:]

Geoffrey Ling MD, PhD, Colonel, US Army (ret) Testimony

Good morning, Chairwoman Eshoo, Ranking Member Guthrie, and Members of the Subcommittee. Thank you for the opportunity to speak before you today and for your consideration of a new federal entity, the Advanced Research Projects Agency for Health or ARPA-H. This is a concept that my colleague, Dr. Michael Stebbins, and I have been working on since 2016. We are delighted to see it gaining momentum with President Biden and the bipartisan support it has received from Congress. I want to acknowledge Mr. Bob Wright and Ms. Liz Feld of the Suzanne Wright Foundation, who have been instrumental in the development and promotion of this momentous initiative.

ARPA-H holds the potential to transform health care and improve health for all Americans and people around the world through the creation of new diagnostics, treatments, and cures. The Committee is well informed of the breadth of support for the creation of ARPA-H. I do wish to point out that Dr. Stebbins and I made the case for ARPA-H (HARPA) in 2019 for the Day One Project and I have provided your staff with a copy of that paper for reference. A cornerstone of our thesis is ARPA-H should be modeled identically on the Defense Advanced Projects Agency (DARPA), the gold standard for innovation.

In order for ARPA-H to revolutionize the discovery and delivery of medical capabilities it needs a revolutionary apparatus. Nothing is more critical to the success of this new agency than getting it right from Day 1, starting with the leadership, authorities, resources, culture, and independence. Retrofitting an existing agency within the government to include ARPA-H will send a message that this approach is merely more of the same, with a different name and some new funding.

While an active-duty Army colonel and after, I served at DARPA for 11 years and was the founding Director of the Biological Technologies Office, a Defense Sciences Office Program Manager, and was named "DARPA Program Manager of the Year" in 2009. DARPA's success developing transformational technological capabilities for national security and everyday life are well known and result directly from its organizational structure and culture. Notable DARPA innovations include the Internet (aka ARPANet), Saturn rocket engine, GPS, night optical vision, portable ultrasound, stealth, robotics, self-driving car, Siri and mRNA genomic vaccines. The "DARPA model" provides an ideal template for ARPA-H.

I would like to focus your attention on one essential aspect of DARPA critical to its success: its independence from larger more established research funding entities in the Dept of Defense. During its inception in 1957, there were efforts by the Army, Navy, and Air Force to fold DARPA into their respective organizations. The Army, Navy, and Air Force were already conducting research and development so certain organizational structures were in place. The rationale was that existing administrative functions such as contracting, legal, and human resource offices could be used to support this new agency. Fortunately, President Eisenhower recognized that if DARPA were to be placed into an existing organization it would be subsumed into an existing culture and thus, nothing would change.

We have an opportunity today, like we have never had before, to build an engine of innovation with the potential to save and improve millions of lives. Industry is on the sidelines waiting for a green light that signals the kind of urgency, accountability, and culture around our health investments that they have seen for DARPA projects.

ARPA-H must be an independent agency within HHS. It must have a reporting structure separate and distinct from the NIH and other agencies. It must have a budget clearly identified and codified into law as separate and distinct from the NIH and the other agencies. Oversight of ARPA-H should come from Congress and not the NIH or any of the other agencies. ARPA-H leadership should hold Director status, with the same rank as the FDA, CDC, CMS, and NIH leaders. Importantly, the ARPA-H Director and senior staff must be term limited to ensure fresh ideas and perspectives are always flowing into the agency.

DARPA's culture is distinct from the other DoD research and development agencies. ARPA-H must have the same innovative culture. The philosophy is to create capability as quickly and efficiently as possible. To do this, it will be a culture of looking for ways to say "yes." It will be a culture of urgency.

It will be a culture of solving problems. How does DARPA do this? DARPA program managers are recruited from everywhere – universities, government, and industry, including start-ups. They serve for pre-determined tenures, at will, which imbues them with urgency and personal responsibility. Risk is rewarded so long as that risk is mitigated by detailed planning, close oversight, and setting clear expectations that involve rewarding success and termination of funding for not meeting performance goals. Program managers must have authority and flexibility in managing their programs to include moving funds from one team to another, terminating contracts for inadequate performance, and bringing in new performers to optimize success. These are core processes that enable DARPA to function as well as it does. An analogy to the DARPA model is professional baseball teams. They will make roster changes during the season, and the teams who made the correct changes will be the ones in the World Series. The accountability for the poor program performance rests with the Program Manager. The accountability of Program Manager performance rests with the Director.

ARPA-H will create new capabilities that cannot be created through other funding mechanisms because they require intense project management approaches that are unique to the DARPA model. These capabilities should be foundational and thus able to solve numerous problems. However, the program itself will be focused on a “use case” to achieve the objective of creating and delivering the capability. An example of an unmet serious problem is the lack of a reliable U.S. solution to the PPE shortage. A DARPA program was created to develop a robot that makes garments such as uniforms. This robot could just as easily make PPE. Another example is ensuring U.S. military’s independence from overseas medicine manufacturing. In 2009, DARPA created a program to develop point-of-care medicine manufacturing to streamline the military’s logistics chain and to alleviate its dependence on a potential peer adversary for any aspect of medicine procurement, including chemical precursors, active pharmaceutical ingredients, or final formulated drugs. This program will result in a “3-D printer” for final formulated medicines that will fit into the back of a Humvee or onto a Blackhawk helicopter to go where the troops go, wherever they are called to serve. DARPA was created to serve DoD. It has stepped in to meet vulnerabilities pertinent to servicemember health. ARPA-H will be created to serve HHS and thus the health of all Americans.

ARPA-H needs to be separate and distinct for fairness. The other agencies do their intended functions well. It is both unfair and unreasonable to expect another agency to change or adapt its culture to enable ARPA-H’s. Every HHS agency should be allowed to do what it does in the manner and with the culture most suitable for their purpose.

ARPA-H has the potential to be another U.S. contribution to the world, and another example of visionary U.S. leadership resulting in improved health and quality of life. However, if ARPA-H is to realize this future, it must be allowed to become what it must, do what it must, and do what is needed. The only way it can accomplish this is by being unencumbered by existing structure, organization, and bureaucracy. It must be separate, distinct and independent.

Thank you.

Ms. ESHOO. Spoken like a general in the Army. Thank you very much.

Next the Chair is so pleased to recognize Dr. Brett Giroir.

You have 5 minutes for your testimony, and welcome again to the subcommittee.

STATEMENT OF BRETT P. GIROIR, M.D.

Dr. GIROIR. Chairwoman Eshoo, Ranking Member Guthrie, subcommittee members, thank you for the opportunity to testify at this historic moment in American history, the creation of ARPA-H.

Long before I became assistant secretary for health, DARPA was my passion. In 1998 I joined a technical assessment council sponsored by DARPA to probe scientific frontiers, and recommended new DARPA initiatives. Five years later, I formally joined DARPA as the deputy director, and then director of the defense sciences office, where I had the honor of working with Dr. Ling. I was the first physician to lead an office at DARPA in its then-50 year history.

On numerous occasions I have assessed concepts for organizations modeled on DARPA. Frequently, these have failed to achieve their potential because of fatal flaws that condemn them to mediocrity. America cannot afford to have a mediocre ARPA-H.

There are two overriding principles that must be the foundation of the agency.

First, at all costs, ARPA-H must nurture a culture of the innovation, where the staff seek transformational advances, not incremental change; where there is no disincentive for failure, only for not being bold enough; where conventional wisdom is generally rejected in favor of novel approaches; where the power of ideas is always more important than a proposal—proposer's institutional brand; and where the goal is to create interactive collaboration, rather than stovepipe competition.

Second, program managers will make or break ARPA-H. The director must have the ability to motivate, attract, hire, and enable program managers from the government, academia, non-profits, and industry. Program managers must be diverse, entrepreneurial, and excel across multiple scientific disciplines.

Next, let me address a few specific issues.

One, I believe it would be a fatal mistake to organize ARPA-H within the NIH. To a great degree, we need ARPA-H because the NIH cannot maintain a culture of radical innovation, disciplined execution, specific accountability, and streamlined processes that are essential for ARPA-H.

Don't misunderstand me. The NIH is outstanding at what it does, but it will never be DARPA or ARPA-H. As such, I strongly support that ARPA-H be independent of the NIH, and that the director report directly to the Secretary of Health and Human Services.

Two, ARPA-H must have rapid, streamlined, and non-burdensome processes to make financial awards within weeks, not months or years.

Three, ARPA leadership must be able to select performers based on the overall likelihood of the program's success. They must be

empowered to select diverse technical approaches and manage overall risks.

Four, with the exception of core business and legal components, ARPA-H staff must have term limits.

Five, like DARPA, ARPA-H must employ disciplined execution. Awardees' progress should be reviewed weekly by program managers, quarterly by office directors, and annually by the director. There are milestones and timelines, and if these are not met the entire agency must address the root causes and attempt to remedy them.

Six, the ARPA-H director must have deep technical knowledge in a field, but by definition cannot be expert in everything that ARPA-H will address. More importantly, the director must be strategic, visionary, and able to recruit the best and the brightest. And needless to say, the director's ability to communicate is paramount.

Seven, the initiatives at ARPA-H must be informed by national priorities, but they must also intersect with scientific opportunities. It may not be possible to "cure stage four cancer next year," but it is possible to develop systems for extraordinarily early diagnosis of multiple cancers at home on a rapid test, enabling early treatment.

In the short term, I believe it is possible for ARPA-H to develop systems to monitor improved health equitably in the home, to prevent falls among the elderly, to dramatically lessen maternal mortality, to develop a new paradigm to solve neurodegeneration, and to shield our Nation from future pandemics.

In conclusion, when the Soviet Union launched Sputnik, the United States channeled its shock into action: DARPA. DARPA has changed the world: the Internet, GPS, stealth, NASA, microelectronics, autonomous vehicles, the bionic arm developed by Dr. Ling, and mRNA vaccines. Much like our Nation's Sputnik moment, it is time for America to admit that the health of our Nation is intolerably poor, that health disparities have worsened, and that we spend far too much to get so little in return. ARPA-H is our best opportunity to catalyze a healthier future for all Americans.

Thank you, and I look forward to your questions.

[The prepared statement of Dr. Giroir follows:]

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WRITTEN TESTIMONY

OF

BRETT P. GIROIR, M.D.

FORMER:

ASSISTANT SECRETARY FOR HEALTH
ACTING FDA COMMISSIONER
ADMIRAL, US PUBLIC HEALTH SERVICE

AND

DIRECTOR, DEFENSE SCIENCES OFFICE, DARPA

BEFORE THE

HOUSE COMMITTEE ON ENERGY AND COMMERCE
SUBCOMMITTEE ON HEALTH

**ARPA-H: THE NEXT FRONTIER OF BIOMEDICAL
RESEARCH**

February 8, 2022

Chairwoman Eshoo, Ranking Member Guthrie, Members of the Subcommittee, thank you for the opportunity to speak with you today about what I believe is an historic and transformational moment in American biomedical research and American history— the creation of ARPA-H – a moment that is both long overdue and desperately needed.

Most of you know me as Admiral Giroir, former Assistant Secretary for Health and Acting FDA Commissioner, and the “Testing Czar” in the Trump Administration. But long before that, in 1998 while faculty at UT Southwestern Medical Center, I became a member of a small technical assessment group sponsored by DARPA. Our group spent months each year probing the frontiers of science, and then providing recommendations for new programs and initiatives to the agency. One of our initial studies led to the development of chlorine dioxide as the first operationally viable gaseous decontamination agent for biological warfare agents – it was later used to decontaminate the Hart Senate Office Building and numerous other facilities after the 2001 Amerithrax anthrax attacks.

Five years later, in late October 2003, I received a call from the DARPA Director, Tony Tether, that the country needed me to leave my tenured university faculty position, my practice of pediatric ICU medicine, and my home, to come to DARPA as the Deputy Director, and eventually the Director, of the Defense Sciences Office. I would have no career there, an uncertain future when my tour was over, a dramatic drop in compensation, family disruption, and the most onerous national security investigation and clearances imaginable; but I would have the chance to serve our nation in a truly unique role, and perhaps change the world in the process. On January 2, I was in Arlington Virginia, at DARPA, for the opportunity of a lifetime. I later became the first physician to lead an office at DARPA in its 50-year history.

During my 4½ years at DARPA, and many times since, I have been involved in assessing and recommending concepts for organizations loosely modeled on DARPA – within the United States government, and also among our global allies. Almost always, these organizations have failed to live up to the achievements of DARPA

because they were created with fatal flaws that condemned them to mediocrity from their inception. America cannot afford to make these mistakes in the creation of ARPA-H.

I am enthusiastic about being here before this subcommittee, because the legislation proposed by Chairwoman Eshoo evidences deep insight into what is critically needed to enable ARPA-H to achieve our nation's extraordinary expectations - to transform public health and medicine, and end centuries of unacceptable health disparities.

Before commenting on a few specific issues, I want to detail several overall principals that must be the foundation of the agency and its operation:

1. At all costs, ARPA-H must nurture and protect a *culture of innovation*, where the Director and program managers seek transformational change, not incremental change; where there is no disincentive for failure, only for not being bold enough; where conventional wisdom and ideas are acknowledged, but almost always rejected in favor of novel hypotheses and orthogonal approaches; where the power of ideas are always more important than a proposer's institutional brand or national influence; where leaders *orchestrate* instead of *manage*; where leaders protect program managers from bureaucratic intrusion and administrative distraction; and where the goal is to create an interactive collaboration among diverse performers around a common goal, rather than stove-piped competition among performers working in their own individual siloes.

2. The ARPA-H Director must have the ability to motivate, attract, hire, and enable diverse program managers from the government, academia, non-profits, and industry. Program managers must be exceptional not only in their scientific expertise in a single field (which may or may not be medicine), but for their ability to work "out of the box" and out of their specific field of expertise. Program managers must be entrepreneurial leaders who spend most of their time roaming the country in search of new ideas and approaches, and building empowered teams who share unbridled passion to achieve the objectives of the program.

DARPA program managers do not look for a reason to reject a proposal, as is the case for many other federal funding organizations; rather, they look for even one key insight or novel approach that could be catalytic for success, and then work collaboratively with the performer to emphasize the strengths and minimize the weaknesses of the proposal. As one DARPA internal quip goes: “An NIH program officer approaches a barn, opens the door, sees that the barn is 6 feet deep in horse manure, is horrified by the smell, screams in disgust, and runs away from the barn. A DARPA program manager opens the same door, sees and smells the same manure, but immediately asks the question, where is the pony?”

Program managers will make or break ARPA-H. They cannot fear failure, only failure to swing for the fences. Program managers at ARPA-H must understand, as I did at DARPA, that if you don’t invent the next Internet, at best you get a “B” on your report card.

3. ARPA-H must have rapid, streamlined, and non-burdensome processes to award grants, contracts, cooperative agreements, and “other transactions” within weeks, not months or years. DARPA uses contracting officers and their technical representatives from throughout the government, from diverse departments, based on their ability to effectively interact with and enable performers. During my tenure, DARPA’s in house contracting shop was only used for the most challenging programs or atypical government performers, and represented only about 10% of total funds expended by the agency.

There are other important principals, but in my experience, these are the most crucial; and the specific legislative authorities and procedures bestowed on ARPA-H by Congress must reflect and operationalize these principals.

Next, let me comment on a few specific issues directly related to pending legislation:

1. In my opinion, it would be a fatal mistake to organize ARPA-H within NIH. To a great degree, we need ARPA-H because the NIH has not, and cannot, create the

culture of innovation, the disciplined execution and managed accountability, and streamlined processes that are required for a DARPA-like agency. This is not to say that the NIH is not outstanding and necessary for what it does – it is. But the NIH will never be DARPA or ARPA-H. As such, I am strongly supportive of Chairwoman’s Eshoo’s legislation that ARPA-H be independent of NIH and that the Director should report directly to the Secretary of HHS. ARPA-H should not be housed on the NIH campus, and perhaps not even in DC. It must be in a place where program managers and their families want to temporarily locate for 4-6 years, near a convenient airport, and in an open environment where performers from academia, non-profits, government, and commercial entities can easily gather and interact with ARPA-H staff and each other.

2. There is a rumor that DARPA does not utilize peer review as part of its selection processes. That rumor is false. DARPA does indeed utilize expert reviewers to evaluate proposals, but unlike NIH, DARPA engages in *peer review* but not *peer decision*. For the most part at NIH, academics from within the specific field form peer review committees. Members on the review committees know the proposers at least professionally if not personally, tend to be highly risk-averse, and essentially rank the proposals by specific *quantitative* scores. With rare exception, a cutoff score is established by available resources; proposals scoring above the line are funded, and those below the line are not.

In contrast, the review process for ARPA-H should look more like the DARPA process. In general, reviewers are technical experts within DARPA and other governmental agencies, not academic peers who work in the field and subject to personal and professional bias and self-interest. At DARPA, proposals were ranked *qualitatively* along several general parameters, not ordered in a regimented rank by specific quantitative scores. Most importantly, the program manager together with the director must be able to select performers based on the overall likelihood of the program achieving its objectives. As such, it is critical to pick a variety of technical approaches and performers with an array of different risks and relative assets, not just the “top five scoring proposals” that may all look

the same, and had been carefully submitted by historically advantaged institutions that have mastered grantsmanship.

3. With the exception of core business and legal staff, ARPA-H staff should have a limited term, and my suggestion is 4 years with an option to renew for another 2 years. When program managers are time-limited, they don't worry about their careers because they don't have a career to begin with. Term limits also create a "hair-on-fire" culture in which program managers know they have a limited time to achieve their dreams, create their legacies, and to change the world. At ARPA-H, there should be no limitations on creativity, no bureaucratic barriers, and essentially no limitations on resources – the only limitation is personal performance during a defined period of time. That is extraordinarily motivating and a "secret sauce" for success.
4. Proposers from academia, industry, and non-profits are, in general, equally eligible to propose to DARPA, and the same should be so for ARPA-H. In my experience, hybrid teams that bring together the best of these diverse sectors are the most successful in achieving aspirational goals. *Teams* should be encouraged by ARPA-H, if not outright required for a majority of programs.

DARPA often leverages informal white papers by proposers in response to a Broad Agency Announcement (BAA). These white papers, written simply and following "Heilmeier's Catechism" (see attachment), serve as the basis for initial discussions and interactions from program managers. They also serve as the basis for teaming; indeed, we frequently had "speed dating" events where potential proposers were brought together in a single room to self-assemble into teams – and sometimes even for DARPA "forced marriages."

White papers can also serve as the basis for seedling funding, which is generally a few hundred thousand dollars available within weeks to jumpstart an idea. The results of seedlings can serve as the basis for advancing an idea or group of ideas into a major program. Once an idea or approach gains traction, then a formal

RFP or BAA is posted and traditional rules for competitive selection are followed.

Once a proposal is selected, unlike for NIH grants, performance of contractors and grantees is frequently reviewed by program managers (weekly), office directors (quarterly) and the director (annually). There are milestones and timelines, and if these are not met, the entire weight of the agency tries to address the root cause and remedy it. ARPA-H can only be successful if the performers are successful. On the other hand, if a project is irretrievably unsuccessful, funding can be stopped and reallocated to alternate approaches.

5. The choice of the ARPA-H Director, especially the inaugural one, will set the tone for the agency; and thus, the choice is a critical one. The Director must have deep technical knowledge in *a* field, but by definition, cannot be expert in everything that ARPA-H will address. The Director must be strategic, visionary, and able to recruit the best and brightest program managers and convince them to completely disrupt their lives for a once-in-a-lifetime opportunity. The ability to communicate up the chain, down the chain, and especially to potential performers across the country is paramount. The Director does not need to be the smartest person in the room, but must be able to discern opportunities and risks, and mentor and enable the creativity of program managers and staff.

An option for the President and Congress might be to place a former DARPA Director, Office Director, or highly successful Program Manager as ARPA-H *Acting Director*, in order to establish the appropriate culture and processes for a limited time until a “permanent Director” can be appointed by the President and/or Congress. There are many individuals with bioscience expertise who were highly successful at DARPA who could potentially fill such a role.

6. The programs and initiatives at ARPA-H must be informed by national priorities, and thus it is vital for the Director and program managers to receive diverse input from federal, state, and local stakeholders – just as we did at DARPA from all

segments of the Armed Forces and Intelligence Community. I do believe the ARPA-H mission should be broad, and approaches to achieving the objectives should be unencumbered by traditional norms.

But national priorities must also intersect with scientific opportunities. It may not be possible to “cure late-stage pancreatic cancer” next year, although it is clearly a national priority; but it may be possible to develop technologies for extraordinary early diagnosis of multiple cancers at home, on a rapid test, and then provide early and curative treatment. I believe it is highly possible to create distributed and equitably accessed technologies to monitor health in the home, prevent falls, diagnose and treat early kidney disease and prevent the need for dialysis, and prevent pregnancy complications that lead to maternal mortality especially among racial and ethnic minorities. These types of initiatives are in the sweet spot for the DARPA process, and can be early wins for the new ARPA-H within its first few years.

7. It is critical to understand what ARPA-H can and should do, and what it cannot. The role of ARPA-H should *not* be to implement and bring to the market preventions or cures. ARPA-H’s role is to develop and prove the *viability* of novel technologies and transformational approaches – to create and sponsor the performance of very high-risk, high-reward research and development – but not to implement it nationally. That is why transition of programs for advanced development is so important. For example, DARPA proved that the prototype F-117 stealth fighter, code-named “Have Blue,” was undetectable by radar. But it looked more like a refrigerator than a fighter jet and indeed could barely fly. Nonetheless, the technical challenge of creating a radar-invisible aircraft was solved. The Air Force took it from there, developed the complex flight controls required, and ultimately made it a formidable and revolutionary combat aircraft. By analogy, once ARPA-H solves the technical barriers for a revolutionary cure, diagnostic, sociological approach, or solution to disparities, the program should be transitioned to other parts of the federal government, for example BARDA or CMS, or for private sector investment to bring it ultimately to the American

people. That type of implementation requires a different skill set and a more management-minded, efficient operation than could ever be done at ARPA-H. After successful program transition, ARPA-H can then refocus on what it is intended to do, and that is, high-risk transformational R&D for another disease or public health challenge.

In conclusion, when the Soviet Union launched Sputnik, the United States channeled our surprise, concern, and technical defeat into action – and thus DARPA was created with a one-page document. DARPA's history of world changing innovation, including the Internet, GPS, Stealth, NASA, microelectronics, autonomous vehicles, the entire field of materials science, mRNA vaccines, and the bionic arm, stemmed from that simple action and its resultant culture of innovation. Much like our nation's Sputnik moment, it is time for America to admit that the health of our nation is intolerably poor, that health disparities have generally worsened for racial and ethnic minorities, the poor, and rural populations, and that we spend far too much to get so little in return. While ARPA-H is not a panacea, it has the realistic opportunity to catalyze revolutionary technologies and approaches that will enable a healthier future for America, and for the entire world.

Thank you for the opportunity to testify today and I look forward to your questions.



Heilmeier's Catechism



George Heilmeier
DARPA Director
1975-1977

- **What are you trying to do?**
 - *Articulate your objectives using no jargon*
- **How is it done today?**
 - *What are the limitations of the current practice*
- **What is new in your approach?**
 - *Why do you think it will be successful*
- **Who cares?**
 - *If you are successful, what difference will it make*
- **What are the risks and payoffs?**
- **How much will it cost? How long will it take?**
- **What are the midterm and final “exams” to check for success?**

Ms. ESHOO. Thank you very much, Dr. Giroir. You really offered compelling testimony to my colleagues and myself.

Next, the Chair is pleased to recognize and welcome Dr. Brian Miller. Dr. Miller—I introduced him earlier, but we love the word “practicing,” practicing hospitalist.

So we are delighted to have you—honored, actually—and extra pleased, because you are here with us in the hearing room. You have 5 minutes for your testimony, Doctor.

STATEMENT OF BRIAN J. MILLER, M.D., M.B.A., M.P.H.

Dr. MILLER. Thank you, Chairwoman Eshoo, Ranking Member Guthrie, and distinguished members of the Subcommittee on Health for inviting me to share my views on biomedical research and ARPA-H, the question for today.

As you mentioned, I am a practicing hospitalist, and my other hat is actually as a health policy researcher. I run a 15-person group, and have experience at four regulatory agencies, which are sometimes barriers to innovation or, at other times, they facilitate it. Today I am here in my own capacity, and my views don’t represent those necessarily of Hopkins or Johns Hopkins Medicine.

I think we all know that innovation—and no one would disagree that innovation is important to us—as consumers or patients, as citizens, as clinicians, and as a country. That is why we spend over \$70 billion in taxpayer funds across ten agencies—more than that, actually; there is quite a list—and \$31 billion through the NIH’s Extramural Grant Program. The private sector accompanies us on this journey, and spends around \$89 billion annually, and venture capitalists join us with an additional \$36 billion.

ARPA-H, as proposed, has multiple challenges, as I see it.

The first is structural. We are duplicating core functions, administrative and otherwise.

The lack of a clear scientific mission and a strategic plan, to me, is most concerning. I have heard all kinds of good visions about things that we can and should do, and agree that we can and should support innovation. However, after meeting with 5,100 stakeholders, the White House should release a clear report identifying the scientific and medical research gaps, along with a strategic plan, before, as my colleagues mentioned, we spend taxpayer money to the tune of \$6.5 billion.

I do agree with all of my colleagues that the basic principles of tenure-limited leadership, and program managers’ managerial independence, and minimal bureaucracy are to be applauded. And in fact, we could think about applying them to some of the existing agencies.

But ARPA-H, even before this, is not enough. China is a rising threat. The biopharmaceutical company market cap of Chinese companies rose from 3 billion to 380 billion, a 100fold increase over the last five years. There were 23 Chinese bioscience IPOs in 2020, and of the world’s largest bioscience IPOs, seven of ten were from China. China has more researchers than we do, and more patents granted it. The Chinese Communist Party has made research and development—and, in fact, dominance thereof with specific GDP targets—a national priority, representing political risk for us. The

Thousand Talents program, launched in 2008, recruited 7,000 scientists, and even featured an ad in Nature Magazine.

So ARPA-H is really not enough if we are going to respond to China. We need to protect our greatest achievement, which is our biomedical research industrial complex. Instead, we should apply the principles that we are talking about here today for ARPA-H to part of a program that we already fund, the NIH Extramural Grant Program, where we invest \$31 billion of taxpayer funds every year.

Let's look to change part of the NIH and the Extramural Grant Program into ARPA-H. Let's have transparency and accountability for indirect costs. Let's have indirect cost reforms to find more funds for researchers without an additional burden on taxpayers, who already face inflation. Let's decrease investigator administrative burdens and, most importantly, that sort of enthusiasm and the three shots of espresso that my colleague Dr. Ling had, as did I, probably, this morning, let's get that into the NIH Extramural Grant Program.

We talk about problems. Well, we all admit that there are problems there. Let's address them.

I also want to say that, in addition to looking at the Extramural Grant Program and just the innovation overall, we can't, you know, ignore regulatory burdens such as the Medicaid Drug Rebate Program or the need for new FDA regulatory pathways for software-driven medical devices and other potential future states.

Thank you, and I look forward to your questions.

[The prepared statement of Dr. Miller follows:]

Testimony of Brian J. Miller, M.D., M.B.A., M.P.H.

Assistant Professor of Medicine and Business (Courtesy)
The Johns Hopkins University School of Medicine
The Johns Hopkins Carey Business School

Before the

U.S. House of Representatives Committee on Energy & Commerce
Subcommittee on Health

On

“ARPA-H: The Next Frontier in Biomedical Research.”

February 8, 2022

Chairwoman Eshoo, Ranking Member Guthrie, and distinguished members of the Subcommittee on Health:

My name is Brian Miller and I practice hospital medicine at the Johns Hopkins Hospital. As an academic health policy analyst I serve as an Assistant Professor of Medicine and Business (Courtesy) at the Johns Hopkins University School of Medicine. My research focuses on how we can make use policy to create a more competitive and vibrant health sector for the benefit of patients. This perspective derives from my experience as a practicing physician, a family member of those who suffered from severe, terminal diseases; and my prior regulatory experience at the Federal Trade Commission, Federal Communications Commission, U.S. Food and Drug Administration, and the Centers for Medicare and Medicaid Services. Through my role as a university faculty member, I regularly engage with regulators, policymakers, and businesses in search of solutions to help create a better healthcare system for all. Today I am here in my personal capacity and the views expressed are my own and do not necessarily reflect those of Johns Hopkins Medicine or Johns Hopkins University.

In my testimony today, I will focus on:

1. The vast federal biomedical research enterprise and why innovation is important
2. The challenges with ARPA-H as proposed
3. A rising China and why ARPA-H is not enough
4. How we can have a strong response to China

1. Innovation and the Federal Biomedical Research Enterprise

Life sciences innovation is important to our country at many levels. As physician, I see and treat patients in the hospital. Each shift I am acutely aware that every drug I prescribe, every diagnostic test ordered, and every device that I or other physicians use has had a long “train of development.” I am thankful that we as a country are wealthy enough to choose to fund and deploy the tools that result from our country’s vast biomedical research enterprise.

Each of us as citizens has or will experience at some point in our lives these products directly ourselves or have them touch the lives of our family members. My late father passed away from glioblastoma multiforme, a rare brain cancer, immediately before I started medical school. His two and a half years struggling with the disease highlighted the benefits of therapeutic innovation – innovation gave him back time that otherwise would have been stolen from him. My mother passed away just last summer from dementia, a disease for which she had no treatment options and where friends and family slowly watch her mind recede. The isolation of the pandemic was broken in her final months by Operation Warp Speed, a public-private partnership launched by previous Administration that resulted in COVID-19 clinical preventive therapeutics. COVID-19 vaccines allowed her friends to visit her in the months preceding her passing, a small saving grace. The pain that individuals and their experience when confronted with a terminal disease for which there is no treatment available along with the benefits of biomedical innovation is well known to me as both a physician and family member.

As a wealthy country we have made a choice to spend a specific portion of our economic resources on healthcare delivery, with half of our annual healthcare expenditures dedicated to hospital and physician services.¹ While the healthcare delivery sector has suffered from the ills of consolidation and monopoly, the life sciences sector has remained vibrant with innovation in prescription and medical devices driving much of how medical care has changed. The treatment of myocardial infarction (MI) – commonly known as a heart attack – represents the benefits of biomedical innovation. Throughout the first half of the twentieth century, the standard of care was bedrest, avoidance of emotional stress, inhaled oxygen, and eventually blood thinners to prevent reinfarction along with nitroglycerine to relieve coronary spasm. Patients rarely resumed usual activity.² In the subsequent decades, both domestic and global medical innovation transformed the treatment of MI, with the development of reperfusion therapy through percutaneous coronary intervention and drug-eluting stents to open up blocked arteries, along with the addition of new

¹ Marin AB, Hartman M, Lassman D, et al. National Health Care Spending In 2019: Steady Growth For The Fourth Consecutive Year. *Health Affairs*. 2021;1:14-24. doi: 10.1377/hlthaff.2020.02022

² Braunwald E. (2012). The treatment of acute myocardial infarction: the Past, the Present, and the Future. *European heart journal. Acute cardiovascular care*, 1(1), 9–12. <https://doi.org/10.1177/2048872612438026>

therapeutics for secondary prevention such as statins for lipid management and beta-blockers and ace inhibitors for blood pressure control.³

Long a competitive global leader in pharmaceutical research and development and sales,^{4,5} American leadership in pharmaceutical product innovation – and medical device innovation too – is a complex multi-factor product of both bench and translational research investment in the private sector and governments shaped by U.S. Food & Drug Administration regulatory policy and payment policy, the latter highlighted by the controversy^{6,7,8} over the debate regarding administrative pricing and potential innovation losses centered around the recently proposed Build Back Better legislation.⁹

A subject of far less debate is the federal government's reach into biomedical innovation. The government's existing reach is vast,¹⁰ covering over ten agencies and over \$70 billion in annual funding (see Appendix).

2. Challenges with ARPA-H as Proposed

Policymakers seeking to promote biomedical research and innovation face many challenges with the proposed ARPA-H structure. Firstly, a strategic plan for the proposed organization's research priorities remains elusive, with proposed legislation noting that ARPA-H director should provide one – including a list of research priorities – either 180 days¹¹ or one year¹² after the agency is established. In the face of over \$70 billion in annual, pre-existing federal biomedical research expenditures and after conducting ten listening sessions¹³ with over 5,100 stakeholders,¹⁴ the administration should make public a list of specific, initial scientific and medical research priorities so that policymakers, federal agency leaders, experts, and the public can understand identified research gaps and evaluate if existing programs can fill this gap.

³ Smith, S. C., Jr, Benjamin, E. J., Bonow, R. O., Braun, L. T., Creager, M. A., Franklin, B. A., Gibbons, R. J., Grundy, S. M., Hiratzka, L. F., Jones, D. W., Lloyd-Jones, D. M., Minissian, M., Mosca, L., Peterson, E. D., Sacco, R. L., Spertus, J., Stein, J. H., Taubert, K. A., & World Heart Federation and the Preventive Cardiovascular Nurses Association (2011). AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients with Coronary and other Atherosclerotic Vascular Disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation. *Circulation*, 124(22), 2458–2473. <https://doi.org/10.1161/CIR.0b013e318235eb4d>

⁴ Grabowski, H. G. (1989). An Analysis of US International Competitiveness in Pharmaceuticals. *Managerial and Decision Economics*, 10, 27–33. <http://www.jstor.org/stable/2487208>

⁵ U.S. International Trade Commission. *Review of Global Competitiveness in the Pharmaceutical Industry*, Staff Research Study #25. 1999. Available from: <https://www.usitc.gov/publications/332/pub3172.pdf>

⁶ Durie, T., Philipson T. (2021). The Evidence Base on the Impact of Price Controls on Medical Innovation. Working Paper No. NO. 2021-108. Becker Friedman Institute for Economics at The University of Chicago. Available from: https://bfi.uchicago.edu/wp-content/uploads/2021/09/BFI_WP_2021-108.pdf

⁷ Holt, C., & Holtz-Eakin, D. (2022, January 13th, 2022). THE POTENTIAL IMPACTS OF THE BUILD BACK BETTER ACT'S DRUG POLICIES. Available from: <https://www.americanactionforum.org/insight/the-potential-impacts-of-the-build-back-better-acts-drug-policies/>

⁸ *Summary of Cost Estimate for H.R. 5376, the Build Back Better Act*. (2021). Washington, DC Retrieved from <https://www.cbo.gov/publication/57627>

⁹ BUILD BACK BETTER ACT, H.R. 5376, 117th Congress (2021).

¹⁰ Breakdown of Science Funding in 2021 Appropriations Request. *American Society for Microbiology* Retrieved from <https://asm.org/Articles/Policy/2020/Breakdown-of-Science-Funding-in-the-President-s-20> (Advocacy, 2020)

¹¹ Cures 2.0 Act, H.R. 6000, 117th Congress (2021)

¹² Advanced Research Project Agency–Health Act, H.R.5585, 117th Congress (2021)

¹³ Proposed Advanced Research Projects Agency for Health (APRA-H). (October 26, 2021). Retrieved from <https://www.nih.gov/arpa-h/events>

¹⁴ *ARPA-H Listening and Feedback Session Summary*. (2021). Washington DC Retrieved from <https://www.nih.gov/sites/default/files/research-training/initiatives/arpa-h/20211020-feedback-summary.pdf>

Culture is paramount, as noted in multiple planning documents.^{15,16} Former NIH Director Francis Collins, M.D., Ph.D., notes challenges with the peer review process that is key to the NIH Study Section grant review process:¹⁷

Another challenge is the peer review process. In theory, peer review, which is having other scientists external to the NIH evaluate and score the proposals, can help ensure that a proposal makes scientific sense and provides value. It is important to integrate peer review into many funding processes because when done appropriately peer review can provide the lens of the scientific community overall. However, when it comes to more unusual and innovative proposals, peer review can be fraught with land mines. The outcome of the review can depend heavily on which specific peers are assessing your application. Scientists can vary substantially in their willingness to entertain new ideas and take risks. Some peer reviewers may be stuck in particular ways of thinking. So if your proposal doesn't resonate with even one of the peer reviewers, it could sink like a pair of cinder block water skis.

Then there are the politics. Peer review can become a bit like the set of the movie Mean Girls, or perhaps more often Mean Boys. The scientific community is full of cliques and social clubs, especially among those who had the same advisors or are in the same narrow field or discipline. There's the risk of reviewers favoring applications from people whom they know and like. Those from more diverse backgrounds, who cross disciplines, or who don't have the "proper" connections may run into walls during peer review too. Ultimately traditional peer review may not always bring fresh new ideas and new people to the table.

As proposed, ARPA-H is to exist as an off-site arm of the NIH, with geographic distance, term limits for the director (5 years) and program managers (3-5 years), and direct oversight of grant administration¹⁸ as ameliorating tactics. While geographic distance and managerial independence have worked to empower some innovation-focused private-sector organizations such as Bell Labs and Xerox PARC, federal government-sponsored results have been more mixed.

DARPA represents a shining example of success having played a key role in the development on ARPANET (the predecessor to the internet), advances in microelectronics, and GPS receivers among other innovations;¹⁹ other federal examples raise significant questions. A more recent example, the CMS Innovation Center, was created in 2010 with a \$10 billion, ten-year budget. Conducting experiments in health finance, the Chief Actuary of CMS has only certified four of over fifty models for national scaling,²⁰ with only two – the Diabetes Prevention Program^{21,22} and components of the Pioneer ACO model – scaled.²³ Market impact has been limited: despite over 16.4 million beneficiaries

¹⁵ Lander, E., & Schwetz, T. (2021). *Advanced Research Projects Agency for Health (ARPA-H): A New Paradigm for Biomedical and Health Research*. Retrieved from https://www.acd.od.nih.gov/documents/presentations/06112021_ARPA-H.pdf See Slide 9 "Culture"

¹⁶ Lander, E., & Collins, F. (2021). *Advanced Research Project Agency for Health (ARPA-H): Concept Paper*. Retrieved from <https://www.whitehouse.gov/wp-content/uploads/2021/06/ARPA-H-Concept-Paper.pdf>

¹⁷ Lee, B. (2021, July 6th, 2021). President Biden Proposes ARPA-H, New \$6.5 Billion Health Entity To Transform How Research Is Done. *Forbes*. Retrieved from <https://www.forbes.com/sites/brucelee/2021/07/06/president-biden-proposes-arpa-h-new-65-billion-health-entity-to-transform-how-research-is-done/?sh=4835aa254dab>

¹⁸ *ARPA-H Frequently Asked Questions*. (2021). Washington DC Retrieved from <https://www.whitehouse.gov/wp-content/uploads/2021/09/092921-ARPA-H-FAQ.pdf>

See page 6, note that final programmatic decisions rest solely with the director, not the program managers.

¹⁹ *DARPA Accomplishments: Seminal Contributions to National Security*. October 2015. Retrieved from <https://www.darpa.mil/attachments/DARPAAccomplishmentsSeminalContributionsToNationalSecurity.pdf>

²⁰ Berwick DM, Gilfillan R. "Reinventing the Center for Medicare and Medicaid Innovation." *JAMA* 325(13):1247-1248.

²¹ *Independent experts confirm that diabetes prevention model supported by the Affordable Care Act saves money and improves health*. (2016) Retrieved from <https://wayback.archive-it.org/3926/20170127185647/https://www.hhs.gov/about/news/2016/03/23/independent-experts-confirm-diabetes-prevention-model-supported-affordable-care-act-saves-money.html>

²² Medicare Diabetes Prevention Program Expansion. Centers for Medicare & Medicaid Services (2016). Available from: <https://www.cms.gov/newsroom/fact-sheets/medicare-diabetes-prevention-program-expansion>

²³ Berwick, DM., Gilfillan, R. (2021) Reinventing the Center for Medicaid and Medicare Innovation. *JAMA*. 2021;325(13):1247–1248. doi:10.1001/jama.2021.3203

estimated to meet eligibility criteria for the Diabetes Prevention Program,²⁴ by 2019 only 200 beneficiaries had enrolled.²⁵

Structural concerns must be addressed. If created as an independent agency, ARPA-H would either have to contract for or directly duplicate many core functions that existing research infrastructure at other federal research enterprises already operate; including program management, policy and planning, financial management, facilities management, and Congressional relations. Further, as proposed, an off-site campus site would be located several miles from the NIH main campus in one of the most expensive real estate markets in the country as opposed to lower cost locales.²⁶

Finally, leadership concerns should be carefully considered. Current legislation proposes that the ARPA-H director be a Presidential appointee.²⁷ However, other core public health agencies such as the NIH have Senate-confirmed heads, with recent legislation proposing that the CDC director be transitioned from a Presidential appointment to a Senate-confirmed position given the agency's sustained struggle across administrations during the pandemic.²⁸ If ARPA-H as proposed fills such a large public health need, Congressional input should be sought in selecting its leader.

3. A Rising China: Why ARPA-H Is Not Enough

A product of political strategy, regulatory reform, and talent recruitment, China's biomedical research investment and the growth of its life sciences industry has far exceeded that of many countries and represents a rising threat to American innovation. Chinese regulatory reform began in earnest in 201 as China's National Medical Products Administration (NMPA) implemented flexible pathways such as accelerated regulatory approval in 2016, with 774 applications received by the end of 2018, followed by the introduction of conditional approval in 2018 for drugs fulfilling unmet needs.²⁹

The corresponding market capitalization of Chinese biopharmaceutical companies has expanded, growing over one-hundred fold, or from \$3 billion in 2016 to \$380 billion in July 2021 and 23 IPOs in 2020, including seven of the ten largest global biopharma IPOs.³⁰ By 2020, over 272 China-based life sciences companies submitted applications for new molecular entities, with recent growth driven by the success of China-based companies as opposed to multinational pharmaceutical companies operating in China,³¹ and many Chinese companies focused on building platform technologies.

²⁴ Meyer H. (2021). Medicare Diabetes Prevention: Enrollment Short Of Projections. *Health Affairs (Project Hope)*, 40(11), 1682–1687. <https://doi.org/10.1377/hlthaff.2021.01292>

²⁵ Tahir, D. (2019). Medicare diabetes prevention program helps a few hundred instead of hundreds of thousands. *Politico*. Retrieved from <https://www.politico.com/news/2019/10/22/medicare-diabetes-lhs-055006>

²⁶ Guzik, B. (2018). Cities with the most affordable office space. *Bizwomen*. Retrieved from <https://www.bizjournals.com/bizwomen/news/latest-news/2018/05/cities-with-the-most-affordable-office-space.html?page=all>

²⁷ Cures 2.0 Act, H.R. 6000, 117th Congress (2021)

²⁸ Prepare for and Respond to Existing Viruses, Emerging New Threats, and Pandemics Act (PREVENT Pandemics Act) - Discussion Draft 117th Congress. (2022) Retrieved from <https://www.help.senate.gov/imo/media/doc/PREVENT%20Pandemics%20discussion%20draft%20sxs%20final.pdf>

²⁹ Le Deu, F., Tang, S., & Zhou, G. (2019). *Biopharma in China: Insights into a market at a crossroads*. Retrieved from <https://www.mckinsey.com/-/media/mckinsey/industries/life%20sciences/our%20insights/biopharma%20in%20china%20insights%20into%20a%20market%20at%20a%20crossroads/biopharma-in-china-insights-into-a-market-vf.pdf?shouldIndex=false>

³⁰ Han, K., Le Deu, F., Zhang, F., & Zhou, J. (2021). *The dawn of China biopharma innovation*. (Page 2) Retrieved from <https://www.mckinsey.com/-/media/mckinsey/industries/life%20sciences/our%20insights/the%20dawn%20of%20china%20biopharma%20innovation/the-rise-of-biopharma-innovation-in-china-vf.pdf?shouldIndex=false>

See page 2

³¹ Han, K., Le Deu, F., Zhang, F., & Zhou, J. (2021). *The dawn of China biopharma innovation*. (Page 5) Retrieved from <https://www.mckinsey.com/-/media/mckinsey/industries/life%20sciences/our%20insights/the%20dawn%20of>

At a societal level, Chinese investment – public and private – in research and development simultaneously is reaching new heights, with China previously targeting a 2.5% of GDP spend on R&D, with public and private science and technology expenditures reaching \$322 billion in 2019.³² Researchers at the Baker Institute examined gross scientific and technical R&D expenditures, educational attainment, patent, and employment trends over the prior decade. They found that Chinese researchers are already exceeding their American counterparts in number and in patents granted, while Chinese gross domestic expenditures on overall R&D are expected to exceed those of the US (see Appendix for Figure). This growth is not accidental, and our trillion dollar “bioeconomy” faces significant global political risk.³³ China’s stated goals of its fourteenth five-year plan emphasize growing links between China’s academic researchers and industry and significant increases in basic science R&D as a share of GDP,³⁴ albeit challenges remain.³⁵

Chinese public and private investment growth and focus has coincided with the growth of the “Thousand Talents” program. Launched in 2008 and the subject of a recent U.S. Senate staff report,³⁶ the Thousand Talents program recruited researchers with salaries, research funding, and infrastructure.³⁷ While the scope within the US remains a source of debate, the program has reached prominent researchers³⁸ such as Charles Lieber, Ph.D., the former Chair of Harvard University’s Chemistry Department.^{39,40}

4. We Need A Strong Response to China

It is within this global context that consideration of domestic biomedical research funding is examined. There is no doubt that the role of the NIH is critical to innovation, with its extramural grant program serving as the agency’s crown jewel. Exploration of the origins of FDA-approved new molecular entities (NMEs) demonstrate this, with one study estimating that all drugs from a 2010 - 2016 were associated with an NIH-funded study at preceding drug targets, representing 20% of NIH funding during that very same period.⁴¹ Other studies found that 6.7% of new drugs

[%20china%20biopharma%20innovation/the-rise-of-biopharma-innovation-in-china-vf.pdf?shouldIndex=false](#) See Page 5

³² Normile, D. (2020). China again boosts R&D spending by more than 10%. *ScienceInsider* doi:doi:10.1126/science.abc5456

³³ Cumbers, J. (2020). China’s Plan To Beat The U.S. In The Trillion-Dollar Global Bioeconomy. *Forbes*. Retrieved from <https://www.forbes.com/sites/johncumbers/2020/02/03/china-now-out-invests-america-in-the-global-bioeconomy-by-30/?sh=1132a0fa7440>

³⁴ Mallapaty S. (2021). China’s five-year plan focuses on scientific self-reliance. *Nature*, 591(7850), 353–354. <https://doi.org/10.1038/d41586-021-00638-3>

³⁵ Bai, A., Wu, C., & Yang, K. (2021). Evolution and Features of China’s Central Government Funding System for Basic Research. *Frontiers in research metrics and analytics*, 6, 751497. <https://doi.org/10.3389/frma.2021.751497>

³⁶ *Threats to the U.S. Research Enterprise: China’s Talent Recruitment Plans* United States. Congress. Senate.

Committee on Homeland Security and Governmental Affairs Retrieved from <https://www.hsgac.senate.gov/imo/media/doc/2019-11-18%20PSI%20Staff%20Report%20-%20China%20Talent%20Recruitment%20Plans.pdf>

³⁷ Jia, H. (2018). WHAT IS CHINA’S THOUSAND TALENTS PLAN? *NATUREJOBS Career Guide: China* Retrieved from <https://media.nature.com/original/magazine-assets/d41586-018-00538-z/d41586-018-00538-z.pdf>

³⁸ Barry, E., & Kolata, G. (2020). China’s Lavish Funds Lured U.S. Scientists. What Did It Get in Return. *The New York Times* Retrieved from <https://www.nytimes.com/2020/02/06/us/chinas-lavish-funds-lured-us-scientists-what-did-it-get-in-return.html>

³⁹ Department of Chemistry and Chemical Biology: Charles Lieber. Retrieved from <https://chemistry.harvard.edu/people/charles-lieber>

Accessed February 4, 2022

⁴⁰ Harvard University Professor Convicted of Making False Statements and Tax Offenses. (2021). *U.S. Department of Justice* [Press release]. Retrieved from:

<https://www.justice.gov/usao-ma/pr/harvard-university-professor-convicted-making-false-statements-and-tax-offenses>

⁴¹ Galkina Cleary, E., Beierlein, J. M., Khanuja, N. S., McNamee, L. M., & Ledley, F. D. (2018). Contribution of NIH funding to new drug approvals 2010-2016. *Proceedings of the National Academy of Sciences of the United States of America*, 115(10), 2329–2334. <https://doi.org/10.1073/pnas.1715368115>

originated in academia or government facilities,⁴² while still other work found that anywhere from 9.3 to 21.2% of new drugs or new indications originated in public-sector research institutions.⁴³ While opinions as the magnitude of the role vary, most policy experts agree that the NIH plays a critical role in funding bench research that serves as the subsequent basis for the private sector's impressive translational research enterprise.

The rise of China and an increasingly competitive global platform for the life sciences industry necessitate that we think bigger. Instead of creating ARPA-H as an independent agency or as an NIH institute, we should instead look to how we can apply the principles and concerns elaborated towards the entire NIH extramural grant program. Taxpayer funds should invest in projects where the "risk is too high, the cost is too large, the time frame is too long, the focus is too applied for academia, there is a need for complex coordination among multiple parties, and the near-term market opportunity is too small to justify the commercial benefit."^{44,45} That is, taxpayer dollars should seek high-risk, high-reward opportunities as opposed to incremental innovation, while at the same time avoid areas of overlap⁴⁶ already targeted by the nearly \$36 billion life sciences investment put forward annually by the domestic venture capital community.⁴⁷

In pursuit of high-risk, high-reward opportunities for taxpayer funds, the ARPA-H proposal notes how DARPA is run by program managers who decide to fund applications or not,^{48,49} as opposed to a peer-review score-based system favored by the NIH study section. Applying a program manager model or adopting the FDA's "professional staff reviewer" model⁵⁰ could promote more rapid decision-making, increase flexibility, and allow for greater discretion and positive "idea risk" in project selection.

In this vein, policymakers may seek to increase funding for researchers to engage in revolutionary research. Luckily, direct research funding may be increased without additional expense to taxpayers. Most NIH grant proposals cover two types of costs: direct and indirect costs. Direct costs⁵¹ include expenses such as salaries, travel, equipment and supplies, or items linked directly to a project. In contrast, indirect costs or facilities and administrative costs,⁵² cover expenses such as buildings, maintenance, and administration. Initially only covering direct costs, indirect costs were

⁴² DiMasi, J. A., Hansen, R. W., & Grabowski, H. G. (2003). The price of innovation: new estimates of drug development costs. *Journal of health economics*, 22(2), 151–185. [https://doi.org/10.1016/S0167-6296\(02\)00126-1](https://doi.org/10.1016/S0167-6296(02)00126-1)

⁴³ Stevens, A. J., Jensen, J. J., Wyller, K., Kilgore, P. C., Chatterjee, S., & Rohrbaugh, M. L. (2011). The role of public-sector research in the discovery of drugs and vaccines. *The New England journal of medicine*, 364(6), 535–541. <https://doi.org/10.1056/NEJMsa1008268>

⁴⁴ *ARPA-H Frequently Asked Questions*. (2021). (Page 1). Washington DC Retrieved from <https://www.whitehouse.gov/wp-content/uploads/2021/09/092921-ARPA-H-FAQ.pdf> See page 1

⁴⁵ Lander, E., & Collins, F. (2021). *Advanced Research Project Agency for Health (ARPA-H): Concept Paper*. Retrieved from <https://www.whitehouse.gov/wp-content/uploads/2021/06/ARPA-H-Concept-Paper.pdf>

⁴⁶ *ARPA-H Listening and Feedback Session Summary*. (2021). Washington DC Retrieved from <https://www.nih.gov/sites/default/files/research-training/initiatives/arpa-h/20211020-feedback-summary.pdf>

⁴⁷ Miller, D. (2021). Record Year for U.S. Venture Capital Industry Despite Pandemic and Economic Downturn [Press release]. Retrieved from <https://nvca.org/pressreleases/record-year-for-u-s-venture-capital-industry-despite-pandemic-and-economic-downturn/>

⁴⁸ Collins, F. S., Schwetz, T. A., Tabak, L. A., & Lander, E. S. (2021). ARPA-H: Accelerating biomedical breakthroughs. *Science (New York, N.Y.)*, 373(6551), 165–167. <https://doi.org/10.1126/science.abj8547>

⁴⁹ *ARPA-H Listening and Feedback Session Summary*. (2021). (Pages 4-6) Washington DC Retrieved from <https://www.nih.gov/sites/default/files/research-training/initiatives/arpa-h/20211020-feedback-summary.pdf> See pages 4-6

⁵⁰ Miller, B., & Richardville, K. (2019). The NIH needs to become leaner and more innovative. Here's how to do that. *Stat News*. Retrieved from <https://www.statnews.com/2019/01/22/making-nih-leaner-more-innovative/>

⁵¹ NIH Grants Policy Statement (2021). Retrieved from https://grants.nih.gov/grants/policy/nihgps/html5/section_7/7.3_direct_costs_and_facilities_and_administrative_costs.htm

⁵² NIH Grants Policy Statement (2021). Retrieved from https://grants.nih.gov/grants/policy/nihgps/html5/section_1/1.2_definition_of_terms.htm#indirect_costs

later included with the rate raised to 8% in the 1940s.⁵³ The history of indirect cost rates⁵⁴ is complex, with a cap of 26% implemented in 1994. However, institutions in some circumstances may also negotiate with the government a specific indirect rate for the institution. A 2015 Government Accountability Office (GAO) study noted challenges with the indirect cost rate-setting process, with three offices – the HHS Cost Allocation Service, the NIH Division of Financial Advisory Services, and the Department of Defense Office of Naval Research – involved in negotiating indirect cost rates for NIH-funded grants.⁵⁵ With indirect grant rates now averaging 52%, over the preceding decade both Republican and Democratic administrations have proposed reforms.⁵⁶

Process reforms could provide significantly increased funding and allow policymakers to help transform the NIH's \$31 billion extramural grant program,⁵⁷ specifically:

1. *Improve accountability*
 - a. Require organizations to specify and make public where indirect dollars flow for all extramural grants using the principles of activity-based costing (i.e. transparency in flow of funds)
 - b. Support HHS OIG oversight of grant-making to ensure appropriate use of funds and protect against problematic project selection.^{58,59}
2. *Decreasing investigator administrative burdens* by simplifying grant application processes and eliminating unnecessary steps such as laudatory references letters,⁶⁰ noting that the grant submission guidance itself is now 153 pages in length⁶¹
3. *Increase available direct research funding* by capping and/or tiering indirect rates
 - a. Caps: mirroring other governmental⁶² or private foundation^{63,64} best practices
 - b. Tiering: create a three tier indirect cost rate policy inversely tied to the institution's rolling three-year average of NIH funding to combat concerns regarding the lack of diversity of funded institutions and investigators^{65,66} and correct the current system which favors wealthy institutions
 - c. Providing transparency of achievements to program managers, in addition to creating innovation-driven metrics of success and failure, both short and long-term

⁵³ Allen, E. (1980). Early Years of NIH Research Grants. Retrieved from <https://history.nih.gov/display/history/Publications?preview=/1016824/8883687/AllenGrantsHistory.pdf#Publication-InstitutionalHistories>

⁵⁴ Rockey, S. (2015). All About Indirect Costs. Retrieved from <https://nexus.od.nih.gov/all/2015/09/11/all-about-indirect-costs/>

⁵⁵ *NIH BIOMEDICAL RESEARCH: Agencies Involved in the Indirect Cost Rate-Setting Process Need to Improve Controls*. Government Accountability Office (2016). Retrieved from <https://www.gao.gov/assets/gao-16-616.pdf>

⁵⁶ NIH plan to reduce overhead payments draws fire. *ScienceInsider* 2017. doi: 10.1126/science.aan6926

⁵⁷ Lauer, M. (2021). *FY 2020 By the Numbers: Extramural Investments in Research*. Retrieved from <https://nexus.od.nih.gov/all/2021/04/21/fy-2020-by-the-numbers-extramural-investments-in-research/>

⁵⁸ Ohio State study: Even healthy cats act sick when their routine is disrupted. (2011). Retrieved from <https://news.osu.edu/ohio-state-study-even-healthy-cats-act-sick-when-their-routine-is-disrupted/>

⁵⁹ Stella, J., Croney, C., & Buffington, T. (2013). Effects of stressors on the behavior and physiology of domestic cats. *Applied animal behaviour science*, 143(2-4), 157–163. <https://doi.org/10.1016/j.applanim.2012.10.014>

⁶⁰ NIH Grant Application: Reference Letter. Retrieved from <https://grants.nih.gov/grants/how-to-apply-application-guide/submission-process/reference-letters.htm>

⁶¹ Research Instructions for NIH and other PHS Agencies (2018). Retrieved from <https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/research-forms-e.pdf>

⁶² Schiermeier Q. (2013). European deal cuts red tape. *Nature*, 499(7456), 18–19. <https://doi.org/10.1038/499018a>

⁶³ Indirect Cost Policy – Bill and Melinda Gates Foundation. (2017). Retrieved from https://docs.gatesfoundation.org/documents/indirect_cost_policy.pdf. The Gates Foundation allows up to a 15% IDC rate for non-government organizations and for-profit organizations, or a 10% rate for universities.

⁶⁴ Indirect Cost Policy – MacArthur Foundation. Retrieved from <https://www.macfound.org/about/our-policies/indirect-cost-policy/>. The MacArthur Foundation assigns a 29% IDC rate.

⁶⁵ Miller, B., & Richardville, K. (2019). The NIH needs to become leaner and more innovative. Here's how to do that. *Stat News*. Retrieved from <https://www.statnews.com/2019/01/22/making-nih-leaner-more-innovative/>

⁶⁶ Pohlhaus, J. R., Jiang, H., Wagner, R. M., Schaffer, W. T., & Pinn, V. W. (2011). Sex differences in application, success, and funding rates for NIH extramural programs. *Academic medicine : journal of the Association of American Medical Colleges*, 86(6), 759–767. <https://doi.org/10.1097/ACM.0b013e31821836ff>

In particular, increasing direct research funding – and decreasing indirect rates in order to do so – could free up over \$2 billion in direct research funds, offering hope for a new generation of researchers, who on average achieve their first R01 grant award now at age 42⁶⁷ in a hypercompetitive marketplace with the number of awardees remaining flat while the number of grant applicants has increased 50%.⁶⁸ Initially, Congress could support researchers through consolidating the authority for institutional indirect rate negotiations for NIH grants in a single office at the NIH, reducing administrative burdens, and implementing rigorous, public transparency requirements for indirect costs. Subsequent reforms focused around the indirect cost rate themselves would need to carefully consider institutional concerns, with ameliorating mechanisms such as a five-year phase-in for new indirect rates to help avoid supply shocks.

4. Conclusions: Supercharging Innovation

One of the great joys of policy regarding biomedical research funding is that it is uniquely bipartisan: everyone is trying to get to the same place, just with different ideas of how best to get there. Biomedical research ultimately powers innovations that are meaningful to us as patients, clinicians, and society as a whole. Both public and private sectors play a key role. The private sector drives translational research, with the pharmaceutical industry alone investing \$89 billion (2019)⁶⁹ while life sciences venture capital poured \$36 billion into the market (2020),⁷⁰ both individually exceeding the size of the NIH's extramural grant program.

As a country we invest over \$70 billion annually in biomedical research across innumerable agencies. While structural, leadership, and strategic challenges remain, the rationale underlying the proposal for ARPA-H highlights many valid concerns present in our nation's federal biomedical research infrastructure. Coupled with the rise of China and a state-sponsored life sciences industry, it is clear that ARPA-H as proposed is not enough for the U.S. to remain the leader in global biomedical innovation.

In order to ensure the continued success of the American life sciences industry, we must think bigger. Reforming the NIH's \$31 billion extramural grant program to transform it along the principles of ARPA-H presents an opportunity to ensure sustainable innovation and growth for the benefit of all Americans. Specific changes providing benefits to taxpayers and relief to researchers include improved transparency, decreased administrative burdens for researchers, and increased direct research funding through modification of indirect costs along with other operational changes. Finally, in addition to sound research funding policy, policymakers must address downstream regulatory barriers to life sciences innovation, such as challenges that the Medicaid Drug Rebate Program presents to valued-based contracting⁷¹ and the need for a new FDA regulatory pathway to provide a less burdensome path to market for software-driven medical devices.

⁶⁷ Rockey, S. (2012) Our Commitment to Supporting the Next Generation. Retrieved from <https://nexus.od.nih.gov/all/2012/02/03/our-commitment-to-supporting-the-next-generation/>

⁶⁸ Lauer, M. (2016) How Many Researchers? Retrieved from <https://nexus.od.nih.gov/all/2016/05/31/how-many-researchers/>

⁶⁹ *Research and Development in the Pharmaceutical Industry*. (2021). Congressional Budget Office. Retrieved from <https://www.cbo.gov/system/files/2021-04/57025-Rx-RnD.pdf>

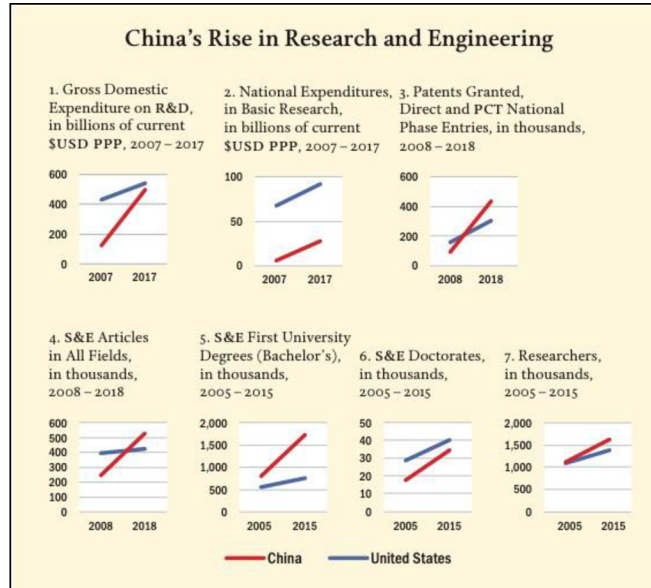
⁷⁰ Miller, D. (2021). Record Year for U.S. Venture Capital Industry Despite Pandemic and Economic Downturn [Press release]. Retrieved from <https://nvca.org/pressreleases/record-year-for-u-s-venture-capital-industry-despite-pandemic-and-economic-downturn/>

⁷¹ Miller, B. J., & Zima, S. C. (2020). Exceptions for Exceptional Cures—Modernizing the Medicaid Drug Rebate Program. *JAMA Health Forum*, 1(8), e201058-e201058. doi:10.1001/jamahealthforum.2020.1058

AppendixFederal Biomedical and Scientific Research Expenditures*

- a. NIH extramural grant program - \$38.3B (out of total \$42.9B)
 - i. \$31.2B is in the enacted budget and \$6.1 billion is in CAREST Act Funding
 - ii. Existing high-risk NIH programs
 - 1. Common Fund - \$0.648B in 2021
 - a. Includes the Director's High-Risk, High-Reward Research Program – \$0.197B
 - i. Early Independence Award - \$21.5M
 - ii. Transformative Research Award - \$38.7M
 - iii. Pioneer Award - \$50.5M
 - iv. New Innovator Award - \$62.4M
 - 2. NCATS - \$0.855B
 - b. BARDA - \$0.597B in 2021
 - c. HHS: Public Health and Social Services Emergency Fund - \$0.209B in 2021
 - d. DoD Basic and Applied Research, Development, Test, and Evaluation Activities – \$8.1B
 - i. DARPA - \$3.50B
 - ii. Armed Forces Research Institute. - \$0.035B
 - e. CDC - \$7.9B
 - f. VA Office of Research and Development - \$0.815B
 - g. USDA – \$1.4B
 - h. Dept of Energy - \$2.4B
 - i. NSF - \$9.1B
 - j. NOAA - \$4.1B
 - k. USGS - \$0.237B
 - l. EPA - \$0.73B
 - m. NASA = \$0.079B
- Sum total annual dollars spent: \$74B (2021)*

*2021 unless otherwise specified. This incomplete list does not include the efforts of other agencies the lack clear budgetary data for research expenditures such as the FDA, the intelligence agencies, and other entities.



Source: Figure 3 from “The Perils of Complacency: America at a Tipping Point in Science & Engineering.” Report Brief, Rice University’s Baker Institute for Public Policy, 2020.

Ms. ESHOO. Thank you, Dr. Miller.

OK, we have heard from all of our panelists, and the Chair recognizes herself for 5 minutes for questions.

Dr. Yamamoto, you have spent and continue to—I mean, you have an illustrious career working with and around NIH. Why do you feel so strongly that ARPA-H should be located outside of the agency?

And I would also like to have Dr. Giroir and Dr. Ling answer that question.

Dr. YAMAMOTO. Thank you for that question. The——

Ms. ESHOO. Perhaps, Dr. Yamamoto, if you could, it would be interesting if you would rebut Dr. Miller.

Dr. YAMAMOTO. Excuse me? I am sorry, I missed what you said.

Ms. ESHOO. To rebut Dr. Miller, whether you agree or disagree, helpful to us.

Dr. YAMAMOTO. But you asked specifically whether—the argument why it should be located outside of NIH. And I think that the main force of that argument is that the mission and goals of ARPA-H are different.

NIH is a masterful agency at discovery of new knowledge, but does not actually extend to being able to develop applications for that new knowledge. And the route for being able to do that has already been cast and demonstrated extremely well in DARPA and in ARPA-E.

Ms. ESHOO. Thank you.

Dr. YAMAMOTO. And so I think that is the reason that it should be outside. Setting up that new culture and operating model within the culture and operating model of NIH, as successful as it is, right, would be challenging, at best. And my fear is that the agency would actually fail, if it were to try to be within the NIH.

Ms. ESHOO. Dr. Ling?

Dr. LING. I was actually——

Ms. ESHOO. You need to turn your microphone on so we can hear your commanding voice.

Dr. LING. I never want to go ahead of a ranking officer.

So anyway, I do believe that ARPA-H needs to be independent.

As we had—we have talked about the construct of this new agency, ARPA-H. To put it inside of NIH—which does its job and does it well—it has created a certain structure, a certain organization, and, of course, a certain culture. That culture has been successful for what it does. We are asking ARPA-H to do something completely different, to take a bold, initial view of things, to do an end-to-end type of approach toward building capability. That is A-number-one. The goal of ARPA-H is to create capability. The role of NIH is to create new knowledge, which it does beautifully.

So when you ask an agency that exists, does their job well, and you subsume another one underneath it, it is going to lose its identity, it is going to lose its structure, it is going to lose its way. So ARPA-H, if it is going to be something new, something bold, something innovative, then it needs to be set free to do exactly that.

And I would point out that we are not doing something brand new, never heard of before. It is following a model that has worked, DARPA. DARPA's model has worked. So that—and so that is really

why I feel passionately that, for ARPA-H to work, it needs to follow the same model.

Ms. ESHOO. Thank you.

Dr. Giroir?

Dr. GIROIR. I completely agree with my colleagues. Tom Brady may be the best quarterback in history, but probably would not have been a good linebacker. The NIH is outstanding at what it does, but it does not have that type of culture, execution, and methodology that an ARPA-H does need.

And look, at DARPA we frequently work with the NIH investigators, right? These are the foundations of the knowledge, that one little glimpse to say yes to people funded by the National Science Foundation, by the Office of Naval Research. These are very complementary and synergistic organizations, but you can't fuse them because you lose the culture of both if you do that.

And again, you cannot condemn ARPA-H to mediocrity from the moment it is born. I feel really strongly, as my colleagues do, that being independent but highly interactive with all the basic research agencies is the way to do this.

Dr. YAMAMOTO. Doctor—Eshoo, Ms. Eshoo, if I may.

Ms. ESHOO. Yes, Dr. Yamamoto?

Dr. YAMAMOTO. If I may, I would just comment on one point made by our colleague, Ms. Krofah, that ARPA-H would be able to work well within the NIH because of the demonstration of ARPA-E being—existing within DoE. And actually, these are non-parallel situations. And Regina Dugan, former DARPA director, has made that point and I think that others have, as well, that the focus of the mission agencies is narrow and really tightly defined.

And so if ARPA-H were in the NIH, it would be like—would be much more like DARPA being within the Air Force. DARPA in the DoD, and so we are talking about ARPA-H being within the HHS.

Ms. ESHOO. The HHS, mm-hmm. Thank you, that is very helpful.

Now I would like to recognize the ranking member of our subcommittee, Mr. Guthrie, for your 5 minutes of questions.

Mr. GUTHRIE. Thank you very much.

And first to Dr. Krofah, my prayers are with your father. You said your father is—in your testimony—struggling with stage four cancer. And you are saying that he hopes that he lives long enough to see his children and grandchildren live their dreams. My guess, if he is watching his accomplished daughter this morning, heavily credentialed, testifying before Congress, he is living one of his dreams. So our thoughts and prayers go with you. And people's personal stories matter, and they bring us forward.

So when we were going to have a previous witness from the White House—and I talked to him this week—one of my questions that we wanted to answer is why was ARPA-H needed, and where should it be, in NIH or outside, and which we are talking about today. And so when we compare DARPA and Sputnik, it appears to me—I wasn't around in the 1950's. I was a child of the—born in the 1960's. But there was really no private sector doing Sputnik, or those types of things.

And so, all of a sudden, we had to put all forces of government to move forward, and which we did this summer with COVID-19 and the mRNA vaccine. And I know that Pfizer and BioNTech used

their experience to develop mRNA cancer vaccines to create vaccines for COVID. So this is for Dr. Miller.

In fact, the company announced in October 2021 they would begin phase two trials in U.S., Germany, Spain, and Belgium to use technology to create colorectal cancer

[sic]. And so the—and in the ARPA-H concept paper, they use this as an example, said if we have ARPA-H, we are going to be able to use—take NIH's research and use mRNA vaccines, an example of transformative projects.

So the question is that is happening in the private sector, and I think Dr. Yamamoto said that we have NIH doing basic research, which we all agree, and then it is executed. That is when we need ARPA-H to execute that research. And so my question, Dr. Miller, is that being done in the private sector? And do we need another government agency to do that? And we are just trying to get to the bottom of that.

Dr. MILLER. Thank you. I agree wholeheartedly. I think that this highlights that we need to actually define what the gap is.

So we have the NIH spending \$31 billion, industry spending 89 billion, the life sciences venture capital community—largely California Research Triangle Park—spending \$36 billion. What are the specific disease targets? What are the specific platform technologies that we see as gaps? We haven't really seen that. I have seen clear suggestions that ARPA-H is a good idea, but not yet a clear strategic priority.

And of course, on top of this, if we are actually going to occupy with a government agency that translational enterprise, we are potentially going to crowd out private sector investment.

Mr. GUTHRIE. So I think an 83 billion in resources through the private sector alone was invested in 2019. How do you see the marketplace, as you just kind of got to, currently adapting to unmet clinical needs?

And what—so there—what we are trying to find—when we talked with Dr. Lander before, it was we have NIH, as we talked about here today, then we have a gap, and then we have the execution in the private sector. So what is the gap? And then, is the gap—how can the gap be filled?

Dr. MILLER. I think the gap is already being filled by the private sector, frankly, and industry. If we look at orphan indications, rare diseases, we now have gene therapy, we have the accelerated approval pathway, which allows early market entry for oncologic therapies for products and disease indications, which people previously had no hope.

I think, if we want to change how we do research, we should think about getting more money out of the indirect costs that we already spend at the NIH in the Extramural Grant Program, rather than burdening taxpayers further.

Mr. GUTHRIE. So Dr. Yamamoto and Dr. Ling, or one of the two of you who have advocated for ARPA-H, would you argue why our—why the private sector isn't filling that, and why ARPA-H is needed to fill the gap? Because you are, obviously, arguing there is a gap. And so why there is a gap, and why the private sector is not filling it.

Dr. LING. There is a gap. There is a gap. There are 10,000 known diseases, there are only 700 cures and treatments. That is a pretty big gap. I am a practicing physician, also. And I am a neurologist, which is the worst. So there is so much in the gap in terms of what I am able to provide patients: Alzheimer's Disease, you can go down the list. I am not going to do that.

There are some very simple things that an ARPA-H could do that do—where the private sector is not filling. The private sector is actually quite conservative. And the point is that early government investment can yield a huge amount of private industry pull.

The trick is going through the valley of death. We have talked about that again and again. And so that is why I am saying that this construct of an ARPA-H is to create that end-to-end, going-forward type of approach. That is really what is needed. You have to de-risk it at each step of the way. We do this at DARPA all the time. You have to de-risk it at each handle. You have to de-risk it for the FDA. You have to de-risk it for the industry. You have to de-risk it for the patients and the clinicians. There is de-risking along the way.

Government support—government, being that they don't have the constraints that the private industry has, for example. I mean, I am a CEO of my own company that I founded. There was a lot of elements to it that government funding does, in fact, really help.

But I will give you a tangible example, a very tangible example, all right? And forgive me, this may take a little bit more than two—

Ms. ESHOO. Yes, you need to summarize, Dr.—

Dr. LING. I will summarize it—

Ms. ESHOO [continuing]. So Dr. Yamamoto can give his answer—

Dr. LING. I will tell you what. I will just yield to Dr. Yamamoto.

Ms. ESHOO. OK.

Dr. LING. I am just going to yield to Dr. Yamamoto, an old friend.

Dr. YAMAMOTO. Thanks, Geoff.

There is a gap. I mentioned the fact that the time between the basic science observation that eventually leads to an FDA-approved drug is 32 years, median time. That is a gap, right? We need to fill that gap, because patients are sick and dying in that—during that period.

Mr. GUTHRIE. OK, I guess I will yield back, and just say I know that some of the 10,000 diseases are still—are at the NIH level, and not moving forward. So I mean, not saying they won't get to the private sector to move forward, as well, and the gap. But thank you so much for your answers, I really appreciate it.

Sorry I went over. I apologize. I yield back.

Ms. ESHOO. You don't have to apologize. Everything that is being discussed is important, and there are so many facets to this.

So the gentleman yields back.

The Chair is pleased to recognize the chairman of the full committee, Mr. Pallone, for your 5 minutes of questions.

Mr. PALLONE. Thank you, Madam Chair—

Ms. ESHOO. And thank you for allowing us to have this hearing.

Mr. PALLONE. It is a consensus.

Dr. Ling, over the course of your career you have participated in and led biomedical discoveries that have transformed medicine, notably your work at DARPA. And you—the stated goal of ARPA-H is to expedite cross-cutting technologies and discoveries like the Genome Project not every 20 or 30 years, but every five to ten.

We have seen the success of programs like DARPA and ARPA-E. But yet engineering systems are not direct comparisons to human biology and complex diseases, so I just want to better understand why ARPA-H is the appropriate model for achieving biomedical breakthroughs, and why now is the right time.

And my first question really expands on what you have already said today, which is, you know, the—what is the gap between the fundamental research and commercial sectors that ARPA-H seeks to fill?

Dr. LING. No, thank you, Congressman.

The—what ARPA-H offers is the opportunity to leverage against the successes of the NSF and the NIH and other agencies that do fundamental research. Biology is not engineering, that is true. But the way to do research can follow a model that does work in engineering.

So a timeline-driven, a milestone-gated, with clear deliverables at the end of a performance period are, in fact, good ways to fundamentally support advancement of R&D so that it can get into and across the valley of death. That is the most important thing. It is not a question of if it is biology or is it chemistry or physics or engineering. It is really of how to manage the research, and how to manage the research dollars.

As Dr.—I gave you an outline of—DARPA takes a very disciplined approach to it, much like ARPA-H must do, as well. To differentiate itself, it must take a very disciplined approach on how the dollars are spent. Milestone-driven, timeline-limited, with clear deliverables: those are the essential elements of success in an ARPA-like construct. And therein lies—so it is not really a question of is this amenable, it is the—it is how the dollars are managed. That is very, very important.

The accountability of that money has to lie with the program manager. The accountability of the program manager lies with the director. And a director's accountability lies, of course, with the Congress, as well as the Secretary of the HHS. There has to be accountability to the money.

Mr. PALLONE. OK. Now, let me just combine my second and third question, which are how will ARPA-H be more effective at advancing cures and treatments for the medical field's biggest challenges, and why is ARPA-H additive, rather than duplicative of existing programs addressing translational research, such as NCATS, if I could combine those two?

Dr. LING. Again, it comes to exactly what I said, it is the process.

So one of the things that, when we set out to do the robot arm that you had heard about, the prosthetic arm, it was that it had to be delivered within four years. There were clear gates to go through it, and so on and so forth. We then achieved it. But at the beginning of that program we had NSF science officers and FDA officers helping review the program, and being part of the program so that, by the time, at the fouryear mark, it was ready to transi-

tion over to going through the FDA regulatory process, we got the arm regulated, fully approved, within eight years of start of program. Eight years, not thirty-three. Eight years. And that arm is now with the Veterans Administration.

So again, we involved the Veterans Administration early on, too, so that they had clinicians and they had patient advocates already going through the steps. That is one example. There is many others, but I don't want to take up your time, Congressman. But I think that that is the point, is that you have to start at the beginning, where you are going to go through all these gates. Plan for them, structure it into the process. And it is the how you spend the money and how you design the program and—to make it a contractual obligation to the performers.

Mr. PALLONE. I appreciate that. I also appreciate your enthusiasm. I can't help thinking about the Super Bowl. Like—you seem like you are, you know, organizing a football team here. It is really great, the energy. Thank you.

I yield back, Madam Chair.

Ms. ESHOO. The gentleman yields back. It is a pleasure to recognize the ranking member of our full committee, Representative Cathy McMorris Rodgers.

You have 5 minutes for your questions.

Mrs. RODGERS. Thank you, Madam Chair.

Leadership matters, accountability matters, character matters, people who do the right thing when nobody's looking, that matters. Unfortunately, I am fundamentally concerned that NIH is not responding to Congress right now. So I will set that aside, because we are focused on ARPA-H right now.

So, Dr. Lander, Dr. Giroir, I would like to start just better understanding how you view what currently is happening at NIH, some of the programs that exist that are intended to be innovative and cutting edge. Congress is funding the Common Fund; the National Center for Advancing Translational Science; High-Risk, High-Reward Program; the Accelerating Medicines Partnership. And that is just at NIH. I would just like to hear you share with me, to share your insights with me as far as are these programs not working, if they are working. Do we still need ARPA-H? And if they are not, should they be eliminated, and these dollars spent part of promoting ARPA-H?

That was Dr.—oh, Dr. Miller. Dr. Miller, sorry. Dr. Miller and Dr. Giroir, if you would answer those questions, please.

Dr. MILLER. Thank you. I guess my question even before that is, you know, with Dr. Ling's comment about program managers and these gated timelines, we have these other programs at the NIH. It sounds like they are not doing that. Why don't we make those NIH programs do that, and transition funding from indirect costs to make a mini-ARPA-H at one of those other programs that are already there?

It sounds like the NIH is also not being responsive. If we think that we have gaps—and there are gaps, and it does take a long time to develop a drug or a device—we should use the existing programs that we have, rather than make a whole new program because we say that the other programs aren't working well. It seems sort of like common sense.

Mrs. RODGERS. OK, thank you.

Dr. Giroir?

Dr. GIROIR. Thank you for that question, and it is a very important one.

ARPA-H is going to be—if so authorized—is going to be a major part of the ecosystem. But it is not the entire ecosystem. As Dr. Ling and others have said, ARPA-H will rely on the basic discovery and ideas that occur at the NIH, at the National Science Foundation, funded by the Gates Foundation, the Leap Fund at Wellcome Trust.

It will also need the kinds of advanced translation that comes out of ARPA-H. ARPA-H will never cure pancreatic cancer; it will create the technical abilities, the novel approaches, de-risk that, so it could be translated and transition to the private sector, and potentially other aspects of NIH, like——

Mrs. RODGERS. OK, if I could just clarify, why do some of these existing programs, that I believe are intended for that same purpose, are not working as intended?

[No response.]

Ms. ESHOO. Dr. Giroir, we lost your audio.

Dr. GIROIR. Sorry. I am going to say that I don't feel I have the ability to comment, you know, extensively on any of these programs currently.

Mrs. RODGERS. OK, OK.

Dr. GIROIR. I certainly have been involved with them, but I can't comment negatively on this program.

Mrs. RODGERS. OK, thank you.

Ms. ESHOO. Yes.

Mrs. RODGERS. And I hear that this agency will be accountable to Congress, yet it is a Presidential appointment without any congressional oversight.

Dr. GIROIR. So——

Mrs. RODGERS. Another question, Dr. Miller. Are there things that we can reform at our existing science agencies, such as NIH and BARDA, to change the culture and the risk tolerance without eroding their core missions?

Dr. MILLER. Absolutely. That is an excellent question. I think having tenure-limited program managers and leadership in various parts of the NIH, in conjunction with making that decision with the NIH director and/or oversight, would be an important transition to happen over time.

Indirect costs, which represent billions of dollars at the NIH, lack of transparency and accountability, and we should demand from funded institutions where that comes—where those dollars are spent.

Mrs. RODGERS. OK, thank you. Well, and I will attempt one more for Dr. Giroir.

I appreciate your perspective here. You know, we are talking about ARPA-H, and that the rules should not be to implement and bring to the market preventions or cures, it should be to develop and prove the viability of these concepts. Can you explain why ARPA-H should be a proof of concept agency?

Dr. GIROIR. Because it really fills—it does fill that gap, it bridges that gap. This is not meant to supplant the private sector or any-

thing down the line, but that gap is real. It needs to de-risk to create new approaches. We don't even have a paradigm for neurodegeneration now. These are the things that it needs to do.

And let me just make a comment. My last year at DARPA I did 113 meetings and briefings. About half of those were to Congress or professional staff, and about half of those were within stakeholder groups. You know, ARPA-H has to have that degree of responsiveness and interaction for it to be successful, and I share your concern about that, and that should be an expectation.

Mrs. RODGERS. OK, thank you. I have more questions, but I have run out of time.

I will yield back. Thank you.

Ms. ESHOO. The gentlewoman yields back.

The Chair is pleased to recognize the gentlewoman from California, Ms. Matsui, for her 5 minutes of questions.

Ms. MATSUI. Thank you very much, Madam Chair, and thank you to everyone who is joining this hearing today to think critically about the future of the biomedical technology pipeline.

Now, there is an ongoing and healthy debate on the appropriate placement of ARPA-H. Generally, there is a consensus that ARPA-H will need an independent structure and novel culture to deliver innovative ideas in health and medicine.

Dr. Giroir, you mentioned ARPA-H needs to be independent, distinct from the traditional NIH institutes and centers. Can you elaborate on how your experience at DARPA helped shape that perspective?

Dr. GIROIR. Thank you very much for that question, ma'am. As Dr. Ling said, it is the whole process of how you do business. It is the whole process and thought process of accountability, but also sort of being a counter-cultural organization that doesn't go with the flow, that doesn't rely on your peers for incremental change.

It relies on teaming, where we bring academia, together with industry, with non-profits, and teams of teams. Nobody really competes against each other. They are competing all for the same goal.

Look, I am a big fan of the NIH. The NIH has done remarkable things for this country. But it could never create the culture that is needed at DARPA. We have a model, as Dr. Ling has said. I do believe it needs to be independent, but it does need to be housed within HHS, the same way as DARPA is within DoD, ARPA-E is within Energy, and ARPA-H should be within HHS.

Ms. MATSUI. Well, can I say this, though? HHS is still a massive agency, with its own levels of bureaucracy, as we know. And acceleration is a key to ARPA-H's mission to transform and improve healthcare. Now, placed at HHS, how can we ensure that ARPA-H has that capability to move quickly and efficiently?

Dr. GIROIR. It really depends on your authorizations. And as I put in my written testimony, I think the legislation by Chairwoman Eshoo has deep insight into the authorities that are needed to make sure that this happens. Picking the first director is going to be critical, allowing rapid contracting, having term limits, being able to hire the best and brightest program managers, and having that independent culture. I really think that legislation provides the basis for what is needed.

This—reporting to the Secretary does not mean the Secretary runs the agency, but it is vital that the director report at the highest level, and I do believe the Secretary is the appropriate level for that.

Ms. MATSUI. OK. Well, thank you very much, Dr. Giroir.

Talking about necessary authorities, DARPA is a unique agency that benefits from numerous special authorities. For example, DARPA can capitalize on flexible hiring and procurement authorities, including grants, contracts, and cooperative agreements, and other transaction authorities. Ms. Krofah, can you explain why special contracting authorities are needed for ARPA-H, and provide an example of when they are best applicable?

[No response.]

Ms. MATSUI.

Ms. KROFAH?

Ms. MATSUI. Yes?

Ms. KROFAH. Thank you, thank you so much for that question. And you know, I want to make a comment, in terms of some of the prior conversation, to say that the momentum for which we are seeing the acceleration and the need for driving innovation is coming out of COVID-19. And we have seen NIH be successful, particularly with a RADx program, in being able to stand up a collaboration with public and private quite quickly.

In terms of your question with other transactional authorities, that is an example where you can leverage such authorities to do hiring, to do contracting in a way where you are not going through significant levels of delay or barriers. That type of authority also needs to be embedded within ARPA-H, including leveraging other hiring practices such as FDA, in bringing top-notch scientists outside of government to play a role in regulatory approval processes.

Ms. MATSUI. OK. Well, that is very good, Ms. Krofah.

I want to quickly touch on a related issue of the critical role that indirect cost recovery associated with NIH grants plays in supporting research at the University of California. From building labs, to quickly processing data, to keeping patients safe, there are indirect but essential costs of conducting research and the Federal Government's support is vital to advancing the research mission.

Dr. Yamamoto, I know you have a long history of helping Congress understand the importance of indirect cost issues. Can you please provide some insight into why research institutions like UCSF receive indirect cost recovery?

Quickly.

Dr. YAMAMOTO. Indirect costs are part of supporting research. Direct costs pay for salaries of the investigators, the equipment that is needed, and so forth. Indirect costs help the institutions to be able to support the infrastructure required for that research to be—take place, whether it is buildings, providing distilled water and electricity, or having administrators who will oversee the grants and make sure that they are managed properly and come into compliance.

So those—so indirect costs have kind of a—have a funny ring to them, because it seems like it is not related to what the investigators are doing. But in fact, those are—those things are crucial. And so they are an important part of allowing the research enterprise

to go forward. Institutions do not recover their full costs of supporting research. Indirect costs provide a portion of that. That is essential.

Ms. MATSUI. OK, thank you very much, Dr. Yamamoto.

I yield back.

Ms. ESHOO. The gentlewoman yields back. The Chair is pleased to recognize the gentleman from Michigan, Mr. Upton, former chairman of the full committee, and one of the authors of Cures 2.0.

Five minutes for your questions.

Mr. UPTON. Well, thank you, Madam Chair.

Nine thousand diseases, five hundred remedies. Every disease group that is out there is looking for that breakthrough therapy. They have got to have the hope to help.

We have got some real champions, bipartisan, on both sides of the Capitol, looking for ARPA-H, knowing that DARPA was so successful, and mainly because they cut through the chaff. They got the job done.

I am not from the Sputnik generation either, but I do remember Lee Iacocca. "Lead, follow, or get out of the way." That is exactly the charge that this organization needs.

So the appropriators have already funded it to billions of dollars if we end up getting out of a continuing resolution. Dr. Giroir, how do we ensure that ARPA-H runs like DARPA? How do we cut through the chaff to make sure that that happens?

Dr. GIROIR. Well, thank you very much, and you are exactly correct.

And I will make another comment. It is not—the money is necessary, but it is not sufficient. You could allocate ten times that amount of money and not achieve the goal, if you don't create the right authorities, the right culture, the right director, the right program managers. I was hired as an IPA from academia, where I was a full professor all these are critically important. But sir, it is all about the culture, and it is all about execution and creating that environment. And that is going to require this committee to protect that environment and the program managers, so they can do exactly what you said which is exactly where it needs to be.

Mr. UPTON. So that is why, to me, that is why we need more than just an appropriation. We need to have the proper oversight and controls to make sure that it runs the way that Lee Iacocca would. Coming from Michigan, he was a good Michigander.

Dr. GIROIR. Yes, sir.

Mr. UPTON. Ms.—he was a great Michigander.

Ms. KROFCHAK. I am so glad the Milken Institute is here. And for those that are watching, or those members that weren't here when we did 21st Century Cures, the Milken Institute just did a wonderful job for us to tap them for ideas to include in 21st Century Cures.

So one of the things that we are looking on in the next version 2.0, is the pandemic response and drug development. I am worried a bit by the current State of the drug development incentives to prevent future pandemics. As you know, Diana DeGette and I are huge proponents of encouraging new antibiotic developments, and

we included our colleague Mr. Doyle's PASTEUR Act in legislation this summer, calling 2.0.

The use of real-world evidence, RWE, has been a big priority. And as—you, as—I want to ask if you are concerned, as I am, about the lack of new antibiotics in the pipeline. And if so, how might RWE or other components of the agreement before us help search for new cures as we look to the—stop a future pandemic?

Ms. KROFAH. Thank you so much, Mr. Upton, for your question. And absolutely, a delight to be here and to partner with you on 21st Century Cures 1.0, and now very supportive of 21st Century Cures 2.0.

I am glad that you brought up the antibiotic issue because, as many of us say, it is silent—that is happening right now. So many are losing their lives to drug-resistant infections.

We do believe that inclusion of the PASTEUR Act is going to play a critical role because, as you know, the market is broken, in terms of our—process for new antibiotics. On the one hand, we want to use fewer antibiotics. On the other hand, because of drug resistance, we need more antibiotics that are able to cut through those particular bacteria.

The challenge, of course, is that we don't have a marketplace that will reimburse innovation at the levels that are needed. PASTEUR will go a long way in ensuring that we are de-linking volume and value, eventually providing incentives along the way that we are supporting innovation tied to the value of those antibiotics, not just prescribing more.

At the same time, we need more than just PASTEUR. We need to ensure that the private sector can be brought in, as well. The Milken Institute has been doing some work around creating innovative financing mechanisms to ensure that we are tying the private sector investment dollars, as well as other incentives such as PASTEUR to make sure it is a level playing field.

You also talked about real world data evidence. We need to collect that wherever they may be found. We need to ensure that they have regulatory grade where they can be used, from decision-making perspectives. So we welcome what we saw during the COVID-19 pandemic. We do think there is much more we need to do to learn from that experience and ensure that we are capitalizing on that antibiotic R&D pipeline.

Mr. UPTON. So do you think we can get to where we ought to be in the next five to ten years?

Ms. KROFAH. Absolutely, if we make sure that we put these incentives in place. We need to make sure that we get PASTEUR over the finish line, absolutely. We need to make sure that we are continuing to invest in these companies upstream. They are doing their best right now, but they are not going to be successful—of course, we saw bankruptcy over time in the antibiotic space. We don't want to continue that trend, so absolutely we . We need to make sure AMR is on the same level as other pandemic preparedness initiatives.

Mr. UPTON. Thank you.

I yield back.

Ms. ESHOO. The gentleman yields back. I just would like to say that it is the intention of the Chair that we move to, you know, leg-

islative and markup on Cures 2.0 and ARPA-H. They are highly complementary of one another.

And you know, when you use the figures 9,000 diseases, 500 solved, we have our work cut out for us, and the people across the country, families, are—they deserve to have hope. Every life is a valuable one. And we always, you know, offer our—not only our sympathy, but our caring to one another when we know something has stricken the family of one of our colleagues. So this is as real as our getting up in the morning and doing our work.

So I think that Congress has the capacity to do this, the wisdom to do it, and that we work hard together to refine whatever needs to be refined, but we should not be in the way of what I just described. So thank you for allowing me the time to say that.

The Chair is really pleased to recognize the gentlewoman from Florida, Ms. Castor, for your 5 minutes of questions.

Ms. CASTOR. Well, thank you, Chair Eshoo, and good morning, everyone. And thank you to our witnesses for their insights today. And I really want to thank Chair Eshoo, and Representative DeGette, and Representative Upton for their leadership. And I look forward to working on this very exciting concept for advanced research projects, the whole initiative that will help us build on the existing research, so that we are not leaving innovative discoveries, treatments, and cures on the table.

But we have to set up this endeavor for success, and I think that includes transparency and accountability. Because, unfortunately, what we have seen over the past two years, data evidence and interventions to address the pandemic have often been met with distrust, outright distrust, and misrepresentation. It has led to poor uptake in the effective and lifesaving interventions such as the COVID-19 vaccine. So for ARPA to succeed, we are going to need to build trust among the public and all of the stakeholders out there.

Stakeholders have specifically requested that ARPA-H be transparent about the selection criteria and the decisionmaking process for its broader investment goals, as well as the selection of individual research projects. So Dr. Ling, what is your perspective on how ARPA-H can be both transparent and accountable?

Dr. LING. Thank you, Congresswoman. It absolutely should be transparent and accountable. It needs to be transparent and accountable at every level, and it begins with the performers. It begins with the scientists and the engineers.

Again, the structure of it is very DARPA-like. And in this case there—it is not a DoD type of project, but it is a health project. So transparency is—absolutely, should be built within the system fully.

So let me be more specific. The performers should be accountable to the program manager. The program managers have the authority to move money around, as well as move the investigator pool around, as well. That program manager is accountable to the office director, and the office director up to the director, and then for—ultimately, the director to the Congress, as well as to the Secretary.

In this whole construct is that—we said before it is going to be a timeline-driven, milestone-regulated process. Those milestones should be very, very transparent. Those should be published, actu-

ally, so that you know exactly what the taxpayers dollars are spent on and, in fact, how well they are doing against those milestones, those phase gates, as it were. And money is tied to it. I will be blunt, money is tied to it. So if they don't perform, they don't get the money. It is real simple.

The other element of this is the engagement. As I said to you before—and I really reiterate this point—engagement has to be just not the investigators. The science is not the end of this. You still have to get through regulatory, you have to get through industry, and you have got to get to the consumer groups, which in this case are the patient advocacy groups, as well as the clinicians that support them.

So at all stages, they have to be engaged from the very beginning, and they have to be engaged throughout the entire process. So that is, in fact, how you build in accountability and how you build in trust, quite frankly. You don't want to bring something in the eleventh hour and say, "Here it is." You want them to be part of the process from the get-go. And in fact—

Ms. CASTOR. Great.

Dr. LING [continuing]. That is how—again, we have a model. It is called DARPA. That is the model, if you look at the BTO, how they do a lot of their medically related portfolio—

Ms. CASTOR. Right.

Dr. LING [continuing]. Because it is a small part of their portfolio. It is still a Defense Department agency. That is why an ARPA-H, which is only devoted to health, is really something that we need here and now.

Ms. CASTOR. OK, thank you.

And Dr. Yamamoto, I was very enthused to see in President Biden's concept paper for ARPA-H he explicitly mentioned the idea of using mRNA vaccines to prevent cancers as an example of potential transformative projects for the new agency. We know the—about the success of mRNA for COVID. Most traditional vaccines take years to develop. Here was a medical miracle, really.

And back home I represent the Moffitt Cancer Center in Tampa, and they are—the researchers there tell me that the mRNA cancer vaccines could potentially be the most—some of the most cost-effective methods for preventing recurrences in the high cost of cancer care. Do you agree, and what do you see as the future here for immunotherapy treatments and prevention?

Dr. YAMAMOTO. Thank you for that question, Congresswoman.

The mRNA vaccines do represent a really revolutionary breakthrough that depended upon years of basic research that came before that to understand the elements that drive stability of messenger RNA, you know, the—inside the cells to be able to create the little packaging molecules that protect the RNA on the way in. And so it was a great victory in that sense.

And your colleagues in Tampa are correct that the potential promise of cancer—mRNA-driven cancer vaccines is enormous, and DARPA had a role in these RNA technologies. So I think that that is correct, and is worthy of all of the excitement that has been generated.

If we step back—and I think it is worth making an explicit point about how the kinds of—the collaborations that come together that

drive the kinds of advances we are talking about. There are about two dozen Federal agencies that are doing science and technology. There is nothing—except for the ARPA models, there is nothing in the mission statements or goals of those agencies that drives them to work together and collaborate.

It is not—there is nothing explicit in the ARPA agencies that say that they should be out talking to all of the agencies around to find out what the capabilities are that could come together to—that would allow them to really make advances. But instead, it is the mission of the program managers and the director that say, “How are we going to get to this really hard point?” And they realize that the only way they can do that is to bring together the talents of other agencies, to bring together—bring in the private sector, and research foundations, and so forth, academia and so forth, to be able to accomplish these goals.

So it is not in the mission statement of the ARPAs to drive collaborations. But the directors know that that is the only way they are going to get there. It is the only way that it is going to work. And so the—so this is a aggregating, convening force that actually does something that no other science agencies in the Federal Government do, to bring together these talents and skills to accomplish hard things.

Ms. CASTOR. Very helpful, thank you.

Ms. ESHOO. The gentlewoman’s time has expired.

Colleagues, I think you have already noticed that I have been very generous with time on both sides of the aisle. But there are excellent questions that are being asked. They deserve to be asked. But we have brilliance here, in terms of our witnesses, and their answers to these questions are just so important. So thank you for indulging my generosity, which I will continue to put out there. How is that? OK.

The Chair is pleased to recognize the gentleman from Virginia, Mr. Griffith, for your 5 minutes of questions.

Mr. GRIFFITH. Thank you very much, Madam Chair. Innovation and medical research has been a priority of mine since I arrived in Congress. I believe there is a role for both the Federal Government and the private sector in this space, and that Congress has a responsibility to fund these activities.

My line of questions that was originally written out said, “OK, tell me why we need a new agency. Let me get my head around this.” You all have answered those questions to a certain extent already, so I am not going to be redundant on this occasion.

But Dr. Ling, you caught my imagination in the spirit of trying to create something new and different. And you said, you know, if we are trying to build—and you used the baseball analogy—if we are trying to get to the World Series, we might like that person a whole lot, but if they are not getting the job done, if they are not performing, we should fire them. But firing people is very difficult at the Federal level, as you know.

So I am interpreting—and I want you to confirm, yes or no, if you agree—I am interpreting that you think, when we pass this legislation, we need to have specific language on, if they are not meeting the requirements of their particular contract, that that

contract will be terminated and they will be fired. Is that correct? Did I understand you?

Mike, so that everybody in the world can hear you.

Dr. LING. Correct, Congressman. In DARPA there is a phrase. It says, "At any time, for any reason, without prior notice, this contract may be terminated at the decision and—of the U.S. Government."

Mr. GRIFFITH. And I appreciate that. And Ranking Member Cathy McMorris Rodgers pointed out, OK, well, what are we talking about with accountability? We need to have some accountability language in there, as well, not just for the executive branch, but also for the congressional branch. Would you agree with that, as well, Dr. Ling?

Dr. LING. There needs to be accountability throughout the system. Exactly, Congressman.

Mr. GRIFFITH. And that would be both executive branch and, two, the Congress of the United States.

Dr. LING. Absolutely. And all the way down to the performer level. They need to feel accountable. This is not their money, it is the taxpayer money.

Mr. GRIFFITH. And we are trying to make sure we get big things done. And if we are going to create a whole new agency inside of our NIH, or inside of whatever we are going—wherever we are going to put it, we need to make sure that they are performing and getting that research done for the American people. I appreciate that very much.

Dr. Giroir, I know you said some good things about the NIH, and I agree. I am involved in some stuff with the NIH. I think they do a great job in their lane, and so forth. But one of the concerns we have had of late is it appears that, through third-party contractors, there is a lot of money being funneled to China. Do you think that we can stop that with ARPA-H?

And should we put some specific language in there that this research needs to be done on American soil?

Dr. GIROIR. Thank you for that. You know, I do believe that the NIH investigators do need to—well, the NIH program managers in NIH offices do need to be more accountable.

In general, if you are an NIH grantee, you get your grant, you put a report together at the end of a year, you send it in, and that is it. And you really don't become accountable until every five years, when that is renewed. Contrast that to DARPA, where, literally, every week the program manager is reviewing the performer. Every month the office director is reviewing all the programs, and every year the director reviews every single [inaudible].

I can also say that, when I was at DARPA—to your staff and the appropriations staff, or from the Defense side, I briefed every single program in my office, what they were doing, and what they were accountable for. That is the degree of transparency and accountability.

So yes, I agree. I do believe the NIH needs to raise the accountability, particularly for overseas investigators, without being burdensome on U.S. investigators. But ARPA-H would be accountable at every level and transparent. That is the nature of the beast.

Mr. GRIFFITH. Well, one of the frustrations that I have had is, in trying to figure out what was going on at the Wuhan lab with American money, was getting answers, and they won't give us the answers. And the—well, I never expect to get answers from the Chinese. And so that creates a problem.

If we are going to spend this money, Dr. Miller, you said, you know, the Chinese are ahead of us on research, they have got all these extra people doing research, and that the United States needs to catch up, and we need to be doing this research, too. What is the point of putting this money into ARPA-H or anything else, if we are then just going to subcontract with the Chinese?

Don't you think we ought to be doing that here, in the United States?

Dr. MILLER. I agree wholeheartedly.

Mr. GRIFFITH. That is what I like, a short, quick answer.

[Laughter.]

Mr. GRIFFITH. Do you—and so we would be a whole lot better off if we were doing that.

And then, if there is some kind of a question of accountability, you would agree, Dr. Miller and both—and Dr. Ling—it is a whole lot easier to get it if we are dealing with people who are in this country and who are answering to us directly, as opposed to a government that does not have any reason to show us anything, or give us any information?

Dr. MILLER. Yes.

Mr. GRIFFITH. Dr. Ling?

Dr. LING. We should only be working with trusted allies and, of course, the United States citizenry. That is exactly what it should be.

Mr. GRIFFITH. Well, and I would say I think it needs to be mostly American. I suppose, if we had a trusted ally that we could actually trust, but when we can't get answers on what happened at Wuhan with American money, I have serious problems about expanding any program that doesn't have language to protect us.

I yield back.

Ms. ESHOO. The gentleman yields back. The Chair is pleased to recognize the gentleman from Maryland, Mr. Sarbanes, for your 5 minutes of questions.

Mr. SARBANES. Thanks very much, Madam Chair. I appreciate the hearing, and I thank the witnesses for their testimony.

There were, I think, 15 listening sessions that were conducted last year, broadly, to invite input around the proposal of ARPA-H. I had a chance to listen to a kind of wrap-up session of that that took place in October. And some of the themes there in describing ARPA-H included positive disruption, establishing benchmarks so that this high-risk, high-reward ambition could be deployed through the opportunity to fail fast. Equity and diversity was a big part of the description of what is being sought through ARPA-H. Use-driven, not curiosity-driven, was a phrase, as well. Measuring success, not through publication, but health improvement for the public, not duplicating existing initiatives, et cetera. And I assume that these are features and characteristics that we saw in DARPA, as well, when it was being developed and obviously now, that it has been deployed.

I wanted to ask Dr. Ling—you and Dr. Yamamoto—to comment on—to put the Human Genome Project and Operation Warp Speed in some context relative to this discussion of ARPA-H, are those efforts ones that, if an ARPA-H had been in place, would have resided there, or would it have been sort of the tip of the spear for those kinds of efforts?

Or are they different in the sense that they were assembling on, at least in the case of Operation Warp Speed, assembling in a kind of emergency fashion existing resources across many different agencies, and therefore they should be distinguished from the kinds of projects that we will see in the ARPA-H space?

But it would be useful to me, as a kind of reference point, for you to make some observations about what ARPA-H would look like, how it would operate, et cetera, against that idea of the Operation Warp Speed or Human Genome, or both.

So why don't we start with Dr. Yamamoto and then Dr. Ling? I would be interested in hearing from you.

Dr. YAMAMOTO. Thank you for that question. Important—an important one.

My view on this is that the two examples that you gave, the Human Genome Project and Operation Warp Speed, if the ARPA-H office had been established, might well have been projects that were carried out under that aegis.

If you remember the way that the Human Genome Project ran, first of all, it took a long time. And second, it turned into this sort of kind of entertaining competition between a private company and the government effort. If ARPA had been in place, that collaboration would have been formed early on, and the progress on the Human Genome Project would have gone much faster. Instead, you had these two camps that weren't communicating with each other, they were collaborating—they were not collaborating, and the work went more slowly.

Operation Warp Speed worked pretty well, and it was in—as you said, in response to an urgent need, right. But Francis Collins himself has said that it was a difficult lift because the culture and practices were not in place at the NIH to really make it work well.

So those examples are actually good examples of things that I think an ARPA structure could be able to accomplish, accomplish well, accomplish better.

Mr. SARBANES. Dr. Ling?

Dr. LING. Yes, I fully agree with Dr. Yamamoto, that the—if there was an ARPA, the opportunity there would have been leveraged much, much earlier.

Let me talk specifically about Operation Warp Speed, which was really—if you take a look at the mRNA vaccines, DARPA had actually invested in this program. It was called the ADEPT program run by my colleague, Dr. Dan—Colonel Dr. Dan Wattendorf, bought back in 2010. And the two performers that he chose was Moderna and GSK. So they were—already, industry was being brought into this ten years before anybody knew that there was a COVID threat around, and they were doing it to develop vaccines against Ebola, actually, at that time.

And so the beauty of this was that they brought in a public-private partnership already at the very beginning, in 2010, 2010—

that—look what it yielded here, now, in 2020, when COVID finally reared its ugly head. And that is why we are talking about—you want to say good gravy, we are really lucky to have an ARPA investment at that time. I think that speaks loudly for it.

And again, let me point out that it was a true private-public partnership. They—it involved laboratories, of course. It involved the FDA, of course. But Moderna and GSK, Moderna and GSK, they were performers in this program.

Mr. SARBANES. Let me ask you, Dr. Ling, since you are speaking now, and I have only got 25 seconds here. But on this discussion around where ARPA-H should be situated, whether it should reside formally inside of NIH or more broadly inside HHS, should it be in the orbit of NIH, either physically or organizationally, be somehow tethered there?

Or do you see it as, in a sense, free-floating within HHS? Can you comment on that a little bit?

Dr. LING. I believe it should be a separate, distinct, and independent agency, just like the CDC is, the FDA is, the NSF, and the NIH. So they are all complementary. They all work together, but they are separate and distinct, and they each have their own chain of command. That is very, very critical.

Mr. SARBANES. Thank you. I yield back.

Ms. ESHOO. The gentleman yields back. The Chair is pleased to recognize the gentleman from Florida, Mr. Bilirakis, for his 5 minutes of questions.

Mr. BILIRAKIS. Thank you, Madam Chair, and I thank all of you for testifying today. Thank you for your patience.

Dr. Miller, you talked in your testimony about the critical need for our Nation to have a strong response to China in the area of biomedical research, and I agree. Rather than focusing on ARPA-H, you say we need to transform the NIH's Extramural Grant Program, which consists of an almost \$32 billion-per-year budget.

One of your reform proposals is to improve accountability and transparency of taxpayer dollars by specifying where indirect dollars go for extramural projects. I couldn't agree more, which is why I introduced the Protecting Integrity of our Biomedical Research Act, which would require disclosure of participation in foreign talent programs as a condition of receiving Federal extramural biomedical research grant dollars.

This was in direct response to cases where—you probably know this—where NIH-funded research had concealed support they had received from the Chinese Government. In fact, the GAO has issued reports stating the need for NIH to address undue foreign influence and increased transparency through disclosure. Despite its direct relevance to research integrity and combating Chinese influence, I am disappointed that the majority decided to ignore my comments in this proposal, and not place it in the COMPETES Act.

Dr. Miller, can you elaborate how adding more transparency requirements to NIH extramural grants will ensure the appropriate use of funds?

And can you give additional ideas of how we can protect against inefficient project selection, please?

Dr. MILLER. Thank you. First and foremost, the average indirect cost rate is around 52 percent. Originally, when the NIH started,

it was around eight percent. The Gates Foundation pays ten percent, and the European Union pays 20 percent. It is unclear to me why our average would be twice that of the EU, or five times that of the Gates Foundation. If a billionaire is getting a better deal than the U.S. Government, that is not exactly a great look for us.

Ways to fix that would include putting a cap, and having tiers, and having a tier tied to your three year prior rolling average, meaning that universities that get more money are in a lower indirect rate group—say, 10, 17.5, 25 percent as an example.

I think the important thing to emphasize is that the current distribution is highly inequitable, where HBCUs and a lot of public schools in the plain states and also the southeast and the southwest don't receive a lot of NIH grants. It is not because there aren't great researchers there, there are. It is just, if you are getting a lot of NIH grants, and you have a lot of administrative funds, you build a massive grant-making apparatus. And then that apparatus helps your researchers compete and comply with the 154-page, I believe it was, guide for NIH extramural grants, right? That takes a lot of infrastructure to respond to that.

So I think that sort of breaking that cycle is a way that we could promote innovation and growth, and also free up funds for direct research funding.

Mr. BILIRAKIS. Thank you. My next question is for Dr. Miller and Dr. Giroir.

I have spent much of my time here in Congress advocating for policies that encourage medical innovation by removing red tape, and incentivizing companies to develop cures as fast, as safe—and safely as possible, particularly for rare diseases. Because of the nature of the 7,000 known rare diseases affecting small patient populations, it often falls through the cracks, unfortunately.

Can you provide examples of how ARPA-H could fill in these gaps and prioritize rare disease research, especially without a specified strategic plan before its creation?

And again, for Dr. Miller and Dr. Giroir.

Dr. GIROIR. Well, thank you—

Dr. MILLER. I will be brief, thank you.

[Pause.]

Dr. MILLER. I was going to say, I will be brief.

We should have a list of what those priorities are before we fund it.

Mr. BILIRAKIS. Thank you.

Dr. Giroir?

Dr. GIROIR. I think, for rare diseases, ARPA-H could be incredibly important.

I am a pediatrician. For example, genetic cures can be remarkable in the future. But if they cost 2 or \$3 million per cure because we have limiting technologies, they are not going to be equitably accessible across the country. So DARPA investing in core types of technologies that can dramatically increase access in an equitable way across a number of rare genetic diseases is just one example that really is biology, but it has an engineering flair, and it is completely there.

We can drive down the cost of cell-based therapies from a half-a-million and a million dollars down tenfold, so we increase the ac-

cess. So these kind of platforms, as opposed to just an individual disease, is where ARPA-H can make an enormous contribution.

Mr. BILIRAKIS. Thank you very much.

I yield back, Madam Chair. Thank you.

Ms. ESHOO. The gentleman yields back. Let me just say to the gentleman the points that you have made about your legislation, which I was not aware of, we will work with you on that, because I think that there are some really important elements relative to transparency and the other things that you raised. So I would be happy to do that.

The Chair is pleased to recognize the gentleman from Oregon, Mr. Schrader, for your 5 minutes of questions.

Mr. SCHRADER. Thank you very much, Madam Chair. I really appreciate this hearing. Very timely, very critical. COVID is shining a light, as some of our witnesses have showed us, on the need for this type of program, going forward, in this very complex world we live in.

I guess the biggest concern I have is, like I said—comment to Dr. Yamamoto—is how do we assure that ARPA-H is not, frankly, just doing the research that industry would do anyway?

I mean, how do we make sure that we are complementary, and assisting, and getting to what industry cannot afford to do, that high risk beyond which they draw the line? How do we evaluate that?

Dr. YAMAMOTO. I think this really depends on the wisdom and insights of the program directors, program managers, to be able to identify de-risking opportunities, areas where industry can't afford to go, or feel that there is not an open—not a big enough market, or that the challenge for getting to—across the valley of death is too great to risk, economically.

And those opportunities are actually all around us. They are really at the heart of why it takes a median time of 32 years to move from a basic research discovery to an approved drug. And so we will be able to find within ARPA-H the program managers that that have identified or maybe even lived those barriers. And it will be—come into ARPA-H.

You know, these program managers, by the way, get their jobs by competing with each other to come to the director of the agency and say, "I have a problem that I think really needs to be solved," right? "And I have a way that I think it can be solved, and here is what it is going to take to get there," right?

And a part of that evaluation and—that the director will make is, you know, what is unique about this? There is something called the Heilmeyer Catechism that says, what is unique about this, where it is not being done elsewhere? And what is it that you think can be done that makes it specifically an ARPA-like project?

Mr. SCHRADER. All right, very good. Thank you. I guess that brings up a second question I had.

I guess Dr. Ling or whoever, I—the question of intellectual property. Would the collaboration between the government and—you know, government equals taxpayer—and industry, which equals shareholder and, you know—how do we allocate the intellectual property rights in those types of collaborations? What has been done?

Mike.

Dr. LING. That has already been legislated, Congressman: the Bayh-Dole Act of 1980, and then the—you know, the Federal regulations, the contract for Federal regulations, are very clear. They—the IP belongs to the private entity. The U.S. Government doesn't make anything. They don't own any factories. So the intellectual property actually belongs to the private entity—

Mr. SCHRADER. Even in case where we are going beyond just basic research?

I understand that argument with basic research. But now that we are going into applied research, should that still apply, in that—

Dr. LING. To my understanding, it does, Congressman.

The one thing that I would point out, though, in all contracts—contracts, not grants, but contracts—is march-in rights. The U.S. Government reserves the right to march in. They can create exceptions that allow them march-in. They can march in because the private partner did not, you know, commercialize it within an X period of time—

Mr. SCHRADER. What, march in, meaning they can acquire those rights?

Dr. LING. Oh, absolutely. They can call—we—at DARPA, we used to call it clawback.

Mr. SCHRADER. OK. OK, very good. I guess my last question is for Dr. Krofah.

That discussed a little bit about we need both NCAT and ARPA-H. They seem—what is the difference, and why do we need both?

Ms. KROFAH. Well, as I mentioned earlier, the broad portfolio for NCATS is actually quite diverse in terms of their reach and activities.

A large part of their portfolio funds the CTSAs. These are the academic institutions that are quite focused on translational research, and that needs to continue. It is about 80 percent of NCATS budget. They help to talk about issues such as de-risking, the value of death, but really a significant way that affects the entire sector, the entire industry.

NCATS also has a program, for example, the—program or the chip for example, and they also have programs for rare diseases. Some of these programs may be appropriate for an ARPA-H-like entity, and others may not be necessarily appropriate for an ARPA-H-like entity. But when we are talking about the point of high-risk, high-reward projects that would be captured under an ARPA-H, those types of projects are quite distinct in supporting the overall field for example of translational sciences, which includes: things like capturing the clinical trial inventory, which happened during COVID-19.

Those—mentioned also contributed data into a platform called—C3, which allowed all of that data that is being generated in these trials and studies and academic settings to be—for COVID-19. Those kinds of programs ought to continue—and may not be the right types of projects for ARPA-H.

Mr. SCHRADER. Very good. Thank you, and I yield back, Madam Chair.

Ms. ESHOO. The gentleman yields back. It is a pleasure to recognize the gentleman from Indiana, Dr. Bucshon, for your 5 minutes of questions.

Mr. BUCSHON. Thank you, Madam Chairwoman. I think most of the questions about ARPA-H have pretty much been answered, so I am going to focus on research, in general.

And in a September letter from numerous biotech and venture capital executives to President Biden, Secretary Becerra, and bipartisan congressional leadership, the executive state—and this is a quote from the letter—“As written, Build Back Better would cause investors and researchers to de-prioritize small molecule drugs for diseases predominantly covered by Medicare, including many cancers and Alzheimer’s.”

Although many of the small companies represented by signatories to this letter will feel that shift in priorities immediately, it will take years for the public and Congress to see the impact of this mistake on the kinds of new drugs that do and don’t come to the market. We can assume that it will take a long time for Congress to come around to fixing its mistake, so BBB could cost us decades of small molecule progress. And I know all too well, as a physician, that eliminating any—even one drug is—has substantial consequences.

So on one hand, some members are stressing the need for additional research and development—and a new department, in fact, or agency—while on the other hand actively working to potentially curtail the industry’s efforts to find new cures through price control-type policies.

So Admiral Giroir, as you know, President Biden recently relaunched his Cancer Moonshot, which I agree with. Considering small molecule oral cancer drugs account for a significant percentage of the biotech industry’s oncology pipeline moving forward, do you share some of the concerns raised by the biotech research and investment community in this letter?

Dr. GIROIR. Well, thank you for the question. I think we have to listen to the biotech community in the letter. Of course, this needs to be overseen by Congress, and really ask the probing questions.

But we cannot—we can absolutely not bias the system against any class of therapeutic, whether it be large molecules, small molecules, biologics, vaccines, types of vaccines. The aperture has to be completely open, and the competition needs to go forward.

So again, I can’t comment specifically on—but you need to listen to industry, and generally—and to ask the right questions. But I—by the fact that they raised it and raised it in such a passionate fashion, I think we need to be very careful about that, because ARPA-H will need to develop small molecules. And in general, they are a lot cheaper, easier to manufacture, and easier to keep on shore than other types of interventions.

Mr. BUCSHON. Thank you. And more broadly, just broadly, do you think that drug price controls will take us backward in cancer research and innovation for patients, and potentially could result in fewer cures discovered if we set Federal-level drug price controls on the industry?

Dr. GIROIR. You know, I am going to give you my own personal feeling here. I think there is a balance that needs to be set, right?

There is a balance that needs to be set, that—and it can be set. It is hard to set it, but, you know, if you have drugs that are too—are not affordable, and people can't have them, it is no use having the drugs. On the other hand, we have seen—and particularly in antibiotics that were brought up—if there is not the proper incentives on that side, then no one will develop it. I do think it is a balance.

Unfortunately, I am not going to give you a simple answer, because it is not a simple answer. Both sides are very valid points, I believe, in my opinion. And this is exactly why we have a committee like yours to work out that balance, because there is.

Mr. BUCSHON. Yes, thank you for that. I mean, it is a difficult policy discussion to have. And you know, the Trump Administration proposed some price control-type things that I disagreed with from that Administration, and I disagree with price controls in general proposed in BBB.

But on the other hand, of course, as you mentioned, patients should have access to drugs, and we need to strike a balance here, and figure out what policies that we can put in place, like some of the bipartisan ones we passed in the last Congress, that can get drug prices down.

I mean, obviously, I am an avid supporter of innovation, and have spent my time in Congress advocating for increased funding for research and development, including at the NIH and other agencies. I think it is important to examine all the different government-funded programs, in addition to the work currently taking place at the NIH, and see how we can, you know, pull or pool our resources together to stretch taxpayer dollars further through better collaboration and assurance that more of the money actually goes toward R&D for innovative drugs, and not toward indirect costs at agencies.

I yield back.

Ms. ESHOO. The gentleman—

Dr. GIROIR. May I—OK.

Ms. ESHOO. Excuse me, did you have something else you wanted to add, Doctor?

Dr. GIROIR. I just wanted to say, from the ARPA-H point of view—and that relates to cost—remember Moore's Law for semiconductors, that every year the capability goes up twofold and it drops by half. That is why your laptop is so relatively inexpensive.

ARPA-H could absolutely do things—like the cost of a genetic cure, just the cost of goods, are a million dollars now. That is why you have to charge \$3 million. ARPA-H could have a program to lower that to 100,000, to decrease that by tenfold, thus increasing access, lowering costs, and helping everyone out. Those are the kinds of things that DARPA—ARPA-H could easily do as part of its mission that will help take the, you know—as an orthogonal approach to drug prices, yes, we need to do what you are doing, but let's lower them across the board by making them more inexpensive because of technologies.

Ms. ESHOO. Thank you, Dr. Giroir. And thank you for quoting my constituent, Moore's Law.

It is a pleasure to recognize the gentleman from California, Mr. Cárdenas, for his 5 minutes of questions.

Mr. CÁRDENAS. Thank you very much, Madam Chairwoman, and I would also like to thank Ranking Member Guthrie. I really appreciate both of you for having this ARPA-H hearing. It is really important for medical innovation and for progress.

Biomedical research is absolutely critical to understanding our most insurmountable medical challenges, and ARPA-H is a particularly exciting opportunity, because it will allow our researchers to investigate with more flexibility, and take on more risk than they can through our more conventional processes.

To me, one of the greatest promises of ARPA-H is its potential to address so many conditions that disproportionately impact communities of color and poor people in America. As we come up on three years of a pandemic that has shown an even brighter light on the glaring health inequities in our country, I am hopeful that ARPA-H could provide a lifeline in the form of treatments, medical devices, and even cures for so many diseases out there.

Dr. Ling, again, thank you so much for sharing your valuable perspective on ARPA-H's incredible potential for a biomedical—for biomedical innovation. How can ARPA-H be leveraged to focus on bridges—bridging the gap in health outcomes across different demographic groups?

Dr. LING. Thank you, Congressman. I would say that it is about what ARPA-H should be about, which is developing capability. Developing capability, that is how you are able to help broadly across the enterprise of not only specific diseases, but also of groups that have been under-represented, you—by being what—the goal of an ARPA-H is not a thing, but a capability, not a particular piece of knowledge, but a capability.

So for example, if you had a much better imaging capability beyond that of MRI, it helps everybody. It helps all diseases. Those are the kind of things that should be an investment of an ARPA-H. DARPA always created capability, and that led to all the other wonderful outcomes that we see today.

Mr. CÁRDENAS. Thank you, Dr. Ling. Also Dr. Ling, is it possible or actually happening out there, where a pursuit of finding a cure could be a company—a private entity could spend \$10 million, \$100 million, or even more, and then, oops, find out that they got at the end of their research and they couldn't find a cure and have to shelve it? Has that happened? Does that happen out there?

Dr. LING. Yes, it does. So the—there is always risk in any endeavor such as this. But the way you manage that risk is through the process.

So we had a saying at DARPA, which I think would apply equally to ARPA, which is, "Fail early, fail fast." And what you do is, by having this gated milestone approach, you can see how you are progressing. You don't want to find out that you are going to lose the race at the end of the race. You want to know along the way that it is not possible to get there.

What it allows you to do is pivot. You don't have to abandon the pursuit of that cure. You might have to pivot. You may say that, oh, a small molecule may not work, I might have to use a large molecule. I may not have to use a large molecule. Surgery, may be more—whatever. But the point is, by having this phased-gate approach, as opposed to just throwing money at the problem, you now

have a way of monitoring accountability of the money, and accountability toward achieving the goal, which is, as you point out, the cure.

But remember, in any of these journeys, if you push the knowledge forward as you do this—you want to push it as fast as you can—you can build on it, even if it looks like you are not going to get there.

Mr. CÁRDENAS. Dr. Ling, it is unfortunate, in my opinion, that in America today some of these innovators, some of these companies, private entities that are investing 100 million, in some cases even \$1 billion, and don't bring something to market, that there is something evil about that.

What is the reality and practicality when an entity has just invested 300 million, 400 million, 600 million, 700 million, and they are just not getting the results to find that cure, for example? Is—does that make them evil for having to figure out maybe it is time to shelve it, and then let's focus on other things?

Dr. LING. Sometimes the science is not there. Sometimes the way it was conducted. There is many reasons for so-called failure, and I think that is—

Mr. CÁRDENAS. So therefore, in our limited time, Dr. Ling, so therefore, is it that ARPA-H will actually help create more opportunities where those investments are—the willing of—the will of those investments can actually result in more cures, more results, more positive results, as you mentioned earlier, having the ability to have this support system, and then shift, and then continue, rather than abandon?

Dr. LING. Absolutely. Absolutely, you can—you—when—we learn mostly from our mistakes. We learn mostly from our failures. It is the pivot and move that becomes very essential. And that is, in fact, the model of an ARPA. An ARPA does exactly that.

Mr. CÁRDENAS. Yes, thank you very much. That is why I have my wife, she definitely reminds me when I make mistakes, and then I learn, and then I [inaudible].

Thank you so much. I yield back.

[Laughter.]

Ms. ESHOO. Dr. Yamamoto, you were nodding. Did you want to add something to this, briefly?

Dr. YAMAMOTO. Yes, I did. Thank you. I would just like to say that the other way that ARPA can contribute to solving the problem that you raised—and a very important one—of a company making a huge investment and coming up with failure, is getting back to capabilities.

Something that Dr. Ling and I talked a lot about when he was founding the BTO was being able to use big—was having DARPA be able to generate computational tools that would allow us to evaluate massive amounts of data that could then be serving, in the case that you are raising, to changing the nature, the size, and the composition of clinical trials.

The more we know about the mechanism behind a given disease that—which can be gathered by, in fact, pulling together lots of data, including real-world evidence—that was raised earlier—the better we are able to be able to construct patient cohorts in clinical

trials that actually have a bigger chance of having the tested drug be successful.

There is great examples of this, but in breast cancer medicine, for example, the first precision medicine drug, if you will, call Herceptin, the drug made by Genentech, a biotech—a small, relatively small, biotech company at that time—was able to structure a clinical trial based on what they knew at the molecular level about the cause of a certain kind of metastatic breast cancer. And by being able to limit the size of that cohort, they were able to carry out a small clinical trial that went relatively rapidly, and succeeded, and Herceptin came out as a drug.

If they didn't have that information, if they hadn't collected that data, they would have had to put together a big trial, with many more patients, and it would have lasted longer. And in fact, we know from Sue Desmond-Hellmann, the president of product development at Genentech during that time, they would not have carried out the trial because it cost, as you said, hundreds of millions of dollars, and it would have failed.

So one of the things that ARPA-H can do is to be able to carry—put together capabilities of that sort that would, in fact, lead to clinical trials that are more—that are successful, and lead to drugs that are successful.

Ms. ESHOO. Thank you. The gentleman's time has expired.

Dr. Yamamoto, it is nice to hear Susan Hellmann's name raised and mentioned.

The Chair is now pleased to recognize the gentleman from Pennsylvania, Dr. Joyce.

Mr. JOYCE. Thank you, Chair.

Ms. ESHOO. Five minutes.

Mr. JOYCE. Thank you, Chair Eshoo, for yielding, and to our witnesses for appearing—

Ms. ESHOO. And happy birthday to you.

Mr. JOYCE. Thank you for the birthday greetings.

Ms. ESHOO. Happy birthday from all of us.

Mr. JOYCE. Thank you, I appreciate that.

Thank you to our witnesses for appearing here today. This is an incredibly important topic.

Dr. Ling, thank you for your passionate testimony on this subject. You have worked at Johns Hopkins. You have worked in academic medicine there. You have worked in the military, and you have worked in the private sector. I think the many prongs that you bring into this equation are very important.

We recently saw a controversial coverage decision from a government agency regarding a breakthrough treatment for Alzheimer's disease, specifically related to amyloid and the deposition of amyloid. How would you envision this ARPA-H agency working with and complementing work being done already with the private sector, and not being resistant to private sector innovation?

Dr. LING. Thank you, Dr. Joyce, and—Congressman Joyce. The drug that you are speaking of, I believe, is the Biogen drug Aducanumab, which was for Alzheimer's, and one of the first to actually show some efficacy against this horrible disease.

So again, I am not privy to understanding the reimbursement decisions, or anything like that, but I can simply say this, is that

comes back to what Dr. Yamamoto just said, and that is developing those capabilities that you can work with a company like Biogen, or you can work with a company like GSK and these others, so that they can better use the data that is available to make it better and easier for them to conduct their clinical trials to be able to save the money up front, to determine more quickly what, in fact, is the benefit.

Because to my understanding of the study right now, is it is—the question is it doesn't work for everybody, but it is very effective in some. And so how do you identify those "some" that could do well? So—because that is true for cancer, that is true for infections. There is always a cohort that seems to do much better from that therapy than, say, another, for whatever reasons it may be.

And elucidating those reasons using new computational capabilities, perhaps using new diagnostic capabilities, all these things within the purview of an ARPA-H to build that capability, Dr. Joyce, so that it can be brought to bear so that then these decisions will have much better evidence to work by, that is the way an R&D agency such as an ARPA would be able to contribute in a positive way to the point that you are making.

Mr. JOYCE. Dr. Ling, you mentioned the research that is necessary. What do you believe can be taken from DARPA and ARPA-E when it comes to securing that research, securing the confidential and sensitive nature of research from nefarious foreign actors?

And how can we do that successfully, while being able to work with the private sector and the academic researchers, all at the same time?

Dr. LING. No, the point you raise is very, very important. You know, these are investments made by the American taxpayer, by the citizenry of our country, and they should be, first and foremost, be to the benefit of the United States.

And I said to you before, and I say it again, that what we are proposing is something a totalitarian government would never propose. That is, having a free and independent agency that would be able to work on behalf of the citizenry. That is totally against what a totalitarian government, such as the adversaries of which we speak of.

As we come back to ensuring that they do this, I think we can take the model of the Department of Defense and DARPA. DARPA agonizes over this all of the time. DARPA agonizes that the things that they create will work their way into an adversarial's arsenal, quite frankly. And so, in many ways, we can learn to use those safeguards and to use those processes that already exist by the model agency that we are working on right now to incorporate them back into an ARPA-H, much as it is in an ARPA defense, which is what DARPA is.

Mr. JOYCE. And I thank you, Dr. Ling, for mentioning the time restraints to achieve these goals, to listen to industry, and we, as Members of Congress, to be responsible stewards of the taxpayer dollars.

Thank you, Madam Chair. Thank you for holding this incredibly important meeting, and I yield the remainder of my time.

Ms. ESHOO. And the Chair thanks you, always, for your thoughtful questions and the—such a respectful way of presenting them. I think we all appreciate that.

The Chair is pleased to recognize another one of the doctors—we are blessed, because we have several doctors as members of this subcommittee, and we benefit from their membership here.

Dr. Ruiz from California, 5 minutes of questions.

Mr. RUIZ. Thank you, Madam Chair, for holding this important hearing.

Over the course of the last two years, the COVID-19 pandemic has exposed the magnitude of health inequities plaguing our country. As a doctor who grew up and practiced medicine in a medically underserved community where health inequities are rampant, I am encouraged that these disparities are at the forefront of our policy conversations. It is imperative that, as we consider the structure and implementation of the ARPA-H program, that we prioritize health equity.

Ms. KROFAH, the Administration is committed to promoting and prioritizing health equity in every decision made by ARPA-H. How can this be achieved, and should such a directive be included in statutory language authorizing ARPA-H?

Ms. KROFAH. Congressman, thank you so much for raising that. You know, when I think about the last two years with the pandemic, it has been absolutely devastating on communities of color, while at the same time there are essential healthcare workers that were suffering disproportionately.

And the issues around health equity are not new, right? We have known these issues for many, many decades, but we have not galvanized the full attention both of government, but also all of our private sector, non-profit sectors, and others to really address this problem. I think we have the unique opportunity to do so now, and I absolutely agree with you that ARPA-H is a model and a vehicle that we should use to really start to understand what is different in the underlying biology of diseases that may affect some populations differently than another.

You know, an analogy that was used the other day that I really appreciated is that, when we think about our clinical trials, it is like testing a car down a straight road and expecting that it is going to perform when conditions change. What we really need to do is to test our products on windy roads, for all populations, to understand when they may not work for subsets of populations.

Mr. RUIZ. Well, I appreciate you saying that, because I have a bill specifically to do just that, Diversity in Clinical Trials Act. Do you think that we need to add statutory language authorizing ARPA-H to do the health equity work?

Ms. KROFAH. I think we need to give the program managers and ARPA-H the flexibility. However, I do think that we need to have a patient advisory board that really provides the diverse representation. That should be written in, where there is consultation in which projects are prioritized.

Mr. RUIZ. And how can we—how can ARPA-H ensure that its workforce is sufficiently diverse?

And how do you see workforce diversity play a role in ARPA-H supporting projects to advance health equity?

Ms. KROFAH. I would agree we need diversity in the program managers, we need diversity in even the director of ARPA-H, and, particularly given that it is time-limited, who those directors will be over time.

We know, particularly at the provider level, that patients are more likely to see people who look like them. We need program managers who look like the communities that are suffering from the burden of disease. So I absolutely agree that part of the considerations for hiring needs to include diversity, and that should be embedded in the legislation.

Mr. RUIZ. Thank you, Ms. Krofah. I am a man of science. I like to measure things. And if you can measure it, then there is a way you can improve it. So how can we measure societal improvements in health equity catalyzed by ARPA-H?

Ms. KROFAH. We need metrics. Earlier we talked about we need a strategic plan. I would add that we need metrics. We need specific metrics for programs that are identified, for which populations may benefit, and for what outcomes we are looking for.

Mr. RUIZ. And how would ARPA-H guarantee that products developed through their pipeline are made available and affordable in an equitable manner to all consumers?

Ms. KROFAH. You know, that is the role of the private sector. We talked a bit earlier about what the private sector offers. They offer that manufacturing, they offer that end to end.

What we need to ensure early on with these high-risk projects with ARPA-H is that we have the ability to reach communities that we are not reaching already. Let's talk about capabilities—

Mr. RUIZ. Well, currently—you know, I understand it is the private sector, but current—in the private sector, often times people who can't afford a certain price are left out of lifesaving remedies that—they have no choice over whether they live or die if they don't get the lifesaving remedy. So government has a role in influencing and incentivizing equity and promotion.

So I hope that, as—Ms. Krofah, that ARPA-H can help advise on ways that we can promote equity like the Biden Administration has done in purchasing some of the vaccines and incentivizing the pharmaceutical companies to use 40 percent in underserved communities.

And with that, I yield back my time.

Ms. KROFAH. Yes, I will just—

Ms. ESHOO. The gentleman yields back.

Ms. KROFAH [continuing]. Comment, just one more—

Ms. ESHOO. Oh, I am sorry.

Ms. KROFAH [continuing]. Comment on that last point, which is just to say that the regulatory piece of the collaboration with ARPA-H is quite critical. We need FDA who's responsible for the review and approval of those products to make sure participants are diverse, and that is what I would add to that.

Ms. ESHOO. Thank you.

The gentleman from Georgia, Mr. Carter—oh, you want to take Mr. Curtis first? Wonderful.

Mr. Curtis, good to see you. You are recognized for 5 minutes for your questions.

Mr. CURTIS. Thank you, Madam Chair, Mr. Ranking Member.

Well, those who know me know I am excited to have another chance to brag about the community in Utah, and our advances in life sciences, and the great things that we are doing there. The Utah BioHive and Utah Health Care System is very active and very healthy. As a matter of fact, BioHive is made up of about 14,000 companies across the State of Utah, and I am really confident that it has been a really dynamic and powerful combination of public-private investment and success.

And I have got to tell you, I am just really pleased with the panel that we have had here today. I have really enjoyed the discussion, and I feel like there is a strong sense that we all want to do something, and we all want to do the right thing, and that we are here to have a thoughtful discussion about what that is. And from the tone of my questions, I wouldn't want anybody to imply that I am opposed to ARPA-H. I just have questions that I want to have resolved in my mind.

Maybe, Dr. Miller, if I could start with you, I am reminded, as we talked today about a famous quote from Ronald Reagan that he made famous, "The most terrifying words in the English language are 'I am from the government, and I am here to help.'" And it feels like sometimes Congress wants to solve all our problems by throwing a lot of money at it, and instead of analyzing maybe what we could be doing to more facilitate what is happening in the private sector.

So I wonder if we should also be talking about less regulation, faster approval process, how removing incentives like I think H.R. 3 does impacts less giving away of IP, as I think we have done with COVID, and less competition. And if I understand some of what has happened today, it almost feels like ARPA-H could come into Utah and compete with some of my private investors, right? Maybe in an IP or otherwise.

So could you just talk about is that a possibility, and what could we be doing to—Dr. Ling, I loved your passion when you talked about unleashing this power, right? But I got to tell you, having spent most of my time in the private sector, I feel the same way about the private sector.

And what can we do, Dr. Miller, to fully unleash the private sector?

Dr. MILLER. Thank you, Representative Curtis, for that question, and good to see you. A couple of things.

First of all, a \$6.5 billion investment in biomedical research does not counterbalance the threat of administrative pricing in drug markets. So the—that doesn't really compute for me.

I think you are right, all—this could potentially, actually, misplace—displace the private sector. I hear phrases like "time-gated", "performance metrics", "fail early," holding program managers responsible. All that sounds like is what I hear my colleagues from pharmaceutical companies and device manufacturers saying. So I worry that ARPA-H will be potentially directly displacing them.

I think we have to look at regulatory barriers, as you said. The Medicaid Drug Rebate Program is one, for example. We have these high-cost, million-dollar therapies, and we want equitable access to them for everybody. Well, the Medicaid Drug Rebate program means that, if you have a value-based contract, and your pharma-

ceutical company doesn't meet the milestone, and the value is zero dollars, that means the price for your drug is zero dollars. So I think we need to address barriers like that.

Mr. CURTIS. Thank you. There has been a pretty healthy debate, but I would kind of like to give Ms. Krofah a chance to weigh in on this, or any of you that would like to, this concept of is the best place for this under NIH.

And I have just got to tell you, from a—here again, from a business perspective, you typically would not put an organization that you wanted very different—under an organization that the culture was so different. So, Ms. Krofah, you seemed to disagree with that. I would love to hear from you, and any of the—else that want to weigh on that that haven't had a chance to express your thoughts on that.

Ms. KROFAH. Yes. Well, thank you so much, Congressman. And I do seem to be in the minority view at least with my panelists on this topic. So I do appreciate you pointing that out.

My perspective comes from a few different places. One is I just experienced coming out of the COVID-19 pandemic. I absolutely agree, in terms of the culture, NIH really is a culture that allows us to do scientific discovery. What we saw differently during COVID was NIH put together public-private partnerships through active through Red X that helped us achieve in, really, a tremendously short amount of time, movement in vaccine therapeutics that really translated into saving of lives.

If we can take those platforms and leverage those learnings, there is an opportunity for ARPA-H to succeed and do well within NIH, but with safeguards. We talked earlier that we need—absolutely we need those safeguards. We need ?

Mr. CURTIS. I—

Ms. KROFAH [continuing]. That there is a level of independence, which—

Mr. CURTIS. I regret that we are out of time, so I am going to cut you off before I get cutoff.

I—once again, before I end, I would just like to thank—the discussion, I think, has been healthy and vibrant, and I appreciate being part of it. Madam Chair, I yield my time.

Ms. ESHOO. The gentleman yields back.

The Chair is now pleased to recognize the gentlewoman from Washington, another one of our wonderful doctors, Dr. Schrier.

Ms. SCHRIER. Well, thank you, Madam Chair, and thank you to our panelists for coming today. I am very excited to talk with all of you about the prospect of ARPA-H. And I think I can speak for all of us when I know just how remarkable it was when the power of the Federal Government joined with private industry to rapidly roll out—develop and roll out coronavirus immunizations. And we had shots in arms in less than a year, and that was remarkable, and it is this sort of power that we are looking to harness in ARPA-H.

This presents such tremendous opportunities, specifically for my home State of Washington, for the researchers who are working on things like CAR-T gene therapies, and precision medicine, and more. And in my State innovative researchers spent more than 8 years pioneering personalized cancer immunotherapies for patients

with lymphoma that hadn't responded to traditional treatment, and that CAR-T therapy represents not just another treatment or the last ditch effort, but is a cure, as we have seen recently, as that immunity lasts a lifetime, and will continue to kill any residual cancer cells that might arise.

I will tell you that another brilliant Washington researcher is studying the ways we might be able to tailor medicine according to individual genomes and phenoms. So using genetic information, coupled with environmental factors, this theory can inform, even from infancy, a child's lifetime risks for disease, and give parents—and then that child later—the tools to mitigate those risks and keep them well.

So, Dr. Yamamoto, I wanted to ask a few things, if you wouldn't mind answering briefly about how ARPA-H could impact just everyday people in Washington State. Like, in your opinion, would ARPA-H be a catalyst for expanding CAR-T gene therapy, maybe to see if it will work in solid tumors?

Dr. YAMAMOTO. Thank you. CAR-T therapy is, in many ways, is powerful and amazing and important, as it is. This is really the tip of the sword for being able to do cell engineering. It enables us to use—develop cell therapies that deliver new therapeutics to the point of action, to the exact cells that are responsible for the disease, for example.

And so I think that there is every possibility that, under an ARPA-like management, that cell therapies could be developed that will definitely be able to serve people throughout your State, and throughout the country, and the world, in fact, because they are—they provide the kind of targeting that allows for early diagnosis, for highly effective therapy early in the state—in disease. And that sort of detection and treatment is really what is needed in order to really counter disease—

Ms. SCHRIER. That is great. And—

Dr. YAMAMOTO [continuing]. Early detection and focused, targeted treatment.

Ms. SCHRIER. And speed is of the essence, right? I mean, eight years to get CAR-T, it is remarkable in one sense, but with the force that we put into Operation Warp Speed, imagine what we could do for, say, pediatric solid tumors, brain tumors, and they just don't have time.

Also, I—

Dr. YAMAMOTO. I will just add that, as a matter of fact, there is a project that UCSF—actually being undertaken right now to be able to use CAR-T therapies in glioblastoma, a very important and devastating brain disease.

Ms. SCHRIER. That is phenomenal. Thank you. I wanted to also ask, in your opinion, as we talk about precision medicine—and I think of this, as a doctor, and who is enrolled in studies. We had to work really hard to get a diverse population in vaccine studies. I was wondering how precision medicine could make a difference, specifically for how health outcomes for women and people of color.

Dr. YAMAMOTO. It is essential that—so precision medicine, as you know, really capitalizes on being able to aggregate and integrate and analyze vast amounts of data about many, many different individuals, right, to be able to gain the knowledge that will allow us

to be able to then take a focused approach to a given disease. And collecting that data then, in a way that is equitable, is very—then becomes very essential.

Clinical trials in this country have not been carried out in an equitable fashion, and it is—and it is the reason that we have found, at the end of the day, disparities that are very damaging. And at the root of them is the failure to be equitable in collecting the information and analyzing it.

Ms. SCHRIER. I only have ten seconds left, so I just want to say, as a pediatrician, how exciting all of this as I think about my patients, patients with autism, patients with threatening diseases—for them we can find cures through something like ARPA-H. So thank you very much. I yield back.

Ms. ESHOO. Thank you, Dr. Schrier. Now, who is next?

OK, the gentleman from Georgia, the pharmacist on our subcommittee, you have five—the only one, too, that is right—you have 5 minutes, Mr. Carter, for questions.

Mr. CARTER. OK, and thank you, Madam Chair, and thank all of you for being here.

I want to start—and bear with me here, before I get into my questions—but it seems like we have a bullying problem with this Administration. I mean, our first witness that was supposed to be here this morning is not here because he resigned last night because of supposedly bullying.

Dr. Fauci, another example of bullying, bullying us into having to take vaccines and having to wear a mask. All examples of bullying.

You look at Dr. Kestner and Dr. Levine bullying Governors into not using monoclonal antibodies, which have been proven to be effective, and then limiting the supplies of those.

The Administration bullied Americans into not using Ivermectin, calling it a horse de-wormer, when actually it has worked for many people, been effective.

And then you have got U.S. Trade Representative Katherine Tai, who has tried to bully American pharmaceutical companies into giving their intellectual property, free of charge, to China.

You know, it just—there is a common theme here, and it is bullying, and it needs to stop with this Administration.

Now that I got that off my chest, Dr. Miller, I want to ask you. You know, we have got a lot of serious public health challenges in this country. There is no question about that. And I recognized that in my 30-plus years of practicing pharmacy. And we need innovation, we need treatment innovation for lymphedema, cancer, hypertension, and all kinds of things. But I am especially concerned about the prevalence of antimicrobial resistance, and the need for new medications. ARPA-H proposals suggest an entirely new department is needed to address the lack of cures and treatments for these issues.

And, I don't know, one of our colleagues on this committee, Morgan Griffith, had recommended a book, "The Perfect Predator." I don't know if you have read that or not, but I am right in the middle of it, and it is a fascinating, true story, a fascinating read. But I will tell you, NIH gives out billions of dollars every year to different agencies, to different companies. And I get it. I understand

what their role is, and what they are supposed to be doing here. But sometimes you have to wonder if we are getting the return on our taxpayers' money that we should be. And it looks like there is a lack of transparency and accountability at the NIH, and it is concerning to a lot of us.

Dr. Miller, what can Congress do, what could we do to reform and modernize the NIH and its mission for advanced research before opening an entirely new department, as is being proposed?

Dr. MILLER. Thank you. I think this brings just a couple core questions to us about sort of how to run a research enterprise. Like my colleagues have all said—and I agree with—you want to minimize bureaucracy, right?

So just blowing that bureaucracy away, why is the grant guide 154 pages long? I mean, that is longer than most people's grants. Could you imagine writing a grant in response to that?

So I think blowing that away, creating a culture of risk tolerance, and that culture of tolerating failure and supporting failure as we think about platforms, as we think about new big ideas, all these principles that my colleagues are mentioning are principles that we should try and integrate into the NIH, and we need to change that culture.

Mr. CARTER. Well, thank you for that. Let me ask you, again—Admiral Giroir, is he with us?

Dr. GIROIR. Yes, he is.

Mr. CARTER. Yes, thank you. I wanted to ask you, I have mentioned my concerns about the prevalence of antimicrobial resistance, the drugs that are currently on the market, and I have certainly witnessed this in my practice of pharmacy throughout the years in the overuse of antibiotics, the lack of pharmaceutical companies investing into research and development for new antibiotics. I believe it is like the early 1980's, the last that we had, and we need to address that. We have got to address that in this country, and I would rather government stay out of it, but at the same time I don't know how we are going to afford not to. We have got to stimulate this in some way.

But looking back on your time at HHS, Admiral, I wonder if you can fill us in on why BARDA and other Federal agencies aren't equipped to address these needs. Is there room for reform at BARDA and NIH and other research programs in the Federal Government to address these type of gaps?

Dr. GIROIR. Well, thank you, and it is good to see you again. And, you know, I am a big pharmacist fan, and I think ARPA-H could do a lot to support pharmacy and distribution of care.

These are fundamentally different organizations. BARDA has turned into—and it is fine—a truly advanced development group on a limited mission set that is for biodefense. So you see investments being made like taking an underlying technology that might have been developed by DARPA, and making sure it gets approval for influenza, or making sure it gets approval for COVID. So it is in a fundamentally different operating space, and I would say its processes are highly bureaucratic, and not really that quick, agile type of program.

On the other end, you have the NIH, which we have discussed very much, so there is, of course, room for reform across the board.

But that bridging of the gap that ARPA-H can do—not to displace the private sector, but to empower the private sector—to decrease risk for the private sector, to create technologies that a rising tide will raise all boats, this is all the kinds of things that ARPA-H will do.

And let me just say, in terms of equity, we talk a lot about cures. Just as you and I talk so much about distributing healthcare by using pharmacists, I think the explicit goal of DARPA should be to get care and prevention in the homes, particularly of the underserved in the world. That may not be as sexy as curing stage four cancer, but it is vitally important, and is along the lines of distributing equitable healthcare and meeting people where they are.

Mr. CARTER. Thank you, Admiral.

And I thank you for your indulgence, Madam Chair, and I yield back.

Ms. ESHOO. Let me just say we have two votes that are up on the floor, so we are going to have to go over to vote.

We have two, four—Mr. Crenshaw came in, that is five, plus a waive-on. Let's take two more members, and then we will recess. I think the—our witnesses need a break, as well. And then we will come back to take the questions of members that have not been recognized yet.

So at this point I will recognize the gentlewoman from New Hampshire, Ms. Kuster, for her 5 minutes of questions.

Ms. KUSTER. Thank you, Madam Chair, and I want to thank all the witnesses for being here today, and for this hearing. I want to take some time to discuss ARPA-H's relationship to existing efforts by the National Institutes of Health.

The NIH has run large, complex programs before, using DARPA-like approaches to drive highly managed, use-inspired, breakthrough research. For example, the NIH Rapid Acceleration of Diagnostics, RADx, initiative utilized an innovative funnel approach to rapidly advance promising COVID-19 diagnostic technologies. Other NIH programs have similar goals to ARPA-H, such as the National Center for Advancing Translational Sciences and the Accelerating Medicines Partnership. The ARPA-H program, then, will need to complement NIH's existing research portfolio, rather than duplicate it, as we have heard in this hearing today.

Ms. KROFAH, can you explain how you see ARPA-H complementing NCATS and other research programs at NIH, and how can its structure avoid redundancies to existing programs?

Ms. KROFAH. Thank you so much for that question. And in fact, you just referenced some good examples from NIH about use-driven research that would be applicable in the ARPA-H context.

I referenced in my prior talk that we need to look at RADx, and the model that was used in RADx, as a potential for what ARPA-H could mean and be in an NIH context. So I agree with you, that those particular case studies—learning from NCATS, learning from AMP, learning from RADx—are absolutely great examples in terms of NIH has performed these types of activities before, and they could be successful in the future, again, with those guardrails that we talked about and the independence that is needed.

Ms. KUSTER. Great. Now, one of the cornerstones of Federal support of research has been around the use of peer review, which

plays a critical role in determining project merit and, ultimately, whether a project is supported.

Dr. Yamamoto, can you speak to how peer review will be leveraged at ARPA-H, and how is it different from the process leveraged by NIH and other Federal agencies?

Dr. YAMAMOTO. Well, if we learn from DARPA, what we know is that there is not actually peer review there, but it doesn't mean there is not review—there is extensive review—and that one of the powers of an ARPA agency will be that it will gain expertise and input and advice, not just from peers, those that are actually carrying out the kind of work that is being proposed, but from across the research spectrum, looking—getting experts from different agencies within the Federal Government, something the NIH doesn't do, and being able then to being able to establish a judgment about the kinds of programs they will undertake, and being transparent about it.

So there will actually be extensive review within the ARPA agency. This is what we have learned from DARPA, very powerful mechanisms that work very, very well.

Ms. KUSTER. Do you think it will be more of a collaboration approach, is that what you are saying?

Dr. YAMAMOTO. Collaborative in the sense that you are bringing voices in from different groups that are not—voices that are not tapped in the NIH peer review system. Remember, that it is an important, I think, distinction to make, that what NIH is trying to do is knowledge discovery, and that—and that the—really, the best way to do that, we now know from many decades of experience, is to give working scientists their own head in—with the problems that they choose to study, using their—the drive of their curiosity to understand something, to do that.

And so peer review of just calling on other fellow scientists to make a judgment about the merits of a given proposal actually works very well. It is—and as Francis Collins has said, it is—does tend to be conservative, because peers are the ones that made the existing paradigms that are going to be defended. They will choose things that are relatively high feasibility, so higher-risk projects are not as well celebrated within the NIH. Those are problems. They are problems that I think can actually be solved by modifying the peer review system.

But the ARPA system actually depends on being able to cast a wide net, get out into the communities, and listen to what is needed, and what is available, and what is possible in order to bring together groups to build the kinds of capabilities that Dr. Ling talks about.

Ms. KUSTER. Well, I think your testimony has been so helpful and important for us today to understand that collaboration is going to be essential, and it is distinct from the other NIH efforts, and I think that is an important distinction.

Thank you, Madam Chair, I yield back.

Ms. ESHOO. We thank you.

Let's see if we can get two more in. Is that all right with you, Brett?

OK.

The Chair is pleased to recognize the gentleman from Texas, Mr. Crenshaw, for your 5 minutes of questions.

Mr. CRENSHAW. Thank you, Madam Chair, and thank you to the ranking member. Thank you to the witnesses for being here for this really important subject. It is fascinating to all of us and I think there is certainly broad agreement that we need to do more to help biomedical innovation and healthcare innovation. There is a lot we can do.

I do have concerns about the ARPA-H proposition, that it may be duplicative, and that it doesn't address some of the problems with innovation, the core problems with CMS, with the FDA. You know, I wonder if that valley of death is really lack of funding or problems with the FDA and CMS not agreeing to pay for a particular project or treatment.

For Dr. Miller, if ARPA-H will cover investment when the private sector fails, we have to ask the question: Why is private sector not investing in a particular product?

OK, so why wouldn't they want to invest in a particular project?

Dr. MILLER. Thank you, Representative Crenshaw. I get proposals from biotech companies and device manufacturers probably every week, and I read them, and usually my answer is no, this isn't going to go anywhere. And it is not necessarily because it is not a good scientific idea, but because, one, there is usually not a payment policy framework for it.

I mentioned the Medicaid Drug Rebate program earlier. That is a common barrier for these sort of curative dream-type therapies that we would like to see that can cure rare diseases.

I think other things are, like at the FDA, we don't have a pathway for software-driven medical devices. And so you are not going to develop that product, because there is no path to market. If we want to turn into the Borg—which, you know would be great, I could run faster, I wouldn't have to worry about getting a knee replacement eventually, and other things—those products aren't there, and no one is going to create them, because you invest hundreds of millions of dollars, years of time, untold thousands of human hours of labor, and then you don't get FDA clearance because the FDA says, "Oh, am I going to evaluate this as AI? Am I going to evaluate this as machine learning? Am I going to evaluate this as software as a medical device? Am I going to evaluate this as a traditional medical device? And should it go through all four offices before it gets cleared?"

So I think a lot of these are regulatory barriers, and we have to address them.

Mr. CRENSHAW. And maybe I will move the question to Dr. Ling.

You know, is there anything in these proposals that would change that?

I mean, what assurances could ARPA-H give to therapeutic developers that their product might be greenlit by regulatory agencies?

Dr. LING. Well, that is a wonderful question, Congressman. Thank you for it.

Part of it, again, comes from—is that there needs to be innovation at all levels. CMS needs to innovate. FDA needs to innovate. CDC needs to innovate. NIH needs to innovate.

Mr. CRENSHAW. OK.

Dr. LING. Within these different groups, to keep up with the 21st century—because that is where we are right now, facing 21st century problems—in fact, you are correct, across the enterprise this needs to be done, but this is where ARPA-H could be very helpful.

Mr. CRENSHAW. I—and I agree. Like, I think there is places for that. But it does seem like the—you know, we might be putting the horse before the cart here, or the cart before the horse. The horse does go before the cart.

[Laughter.]

Mr. CRENSHAW. Anyway, you know what I mean.

Maybe—and help us paint a picture, Dr. Ling, of, if ARPA-H was created right now, in your perfect vision, do you have any examples of some projects that it could immediately undertake?

I mean, who out there, what startup out there right now, is just waiting for investment, but just can't get any?

Dr. LING. Thank you, Congressman. One project I think that would be very helpful, to be illustrative, is what I came back to before, is imaging.

So right now—in the 1920's, we came with X-ray, great. In the 1960's we came up with CT scan, great. In the 1980's we came out with MRI, super duper. What has happened since then? Nothing.

So an ARPA-H project would be get me an imaging platform that would have performance metrics at least an order of magnitude better than MRI. Boom. Make it so that it has to operate at room temperature. That drives cost down. Make it so that it is not using ionizing radiation, much as X-ray and CT do, so it doesn't hurt patients. What technologies can bring to bear that you can do this right now?

And I am a geek, all right? So, for example, quantum orbital resonance spectroscopy could be an example. What you want—and there are small groups doing it right now, they can't get the money to do it. Siemens doesn't want to do it. Why? Because they sell MRIs. Why in heaven's name would they do that? So it is a white space. It is a technological solution.

Now, what would be the benefit of doing such a thing, you would ask, Congressman. Well, if you had an order of magnitude better performance, you could actually diagnose cancer earlier. And I don't mean just a cancer. I mean, all cancers. Then you now have the opportunity of treating cancers when in stage one and stage two. We may not have to invent new drugs. We may actually improve health because we are able to—that is an example of building a capability.

Now, you talked about the regulatory on that. You need to drag the FDA in, right then and there, as we start, and say, "Look, this is coming. You need to come up with ways to regulate this. That is your job." But they—but you can't bring it to them 4 years later, after it is done, and say, "Now you have got to do it." You have got to bring them in on day one. That is the point I am trying to make, is that that end-to-end solution—and ARPA-H would call that—as much as Dr. Yamamoto said, you have got to bring these groups together now, early.

You have got to bring the patients in, because they are not going to want to lie down in this thing if they don't understand what the

heck it is. So you have got to bring them in early, early, early. You have got to bring them in at the very outset, Congressman. That is, in fact, how DARPA does it. It doesn't tell the Marines you are going to have this new thingamajig. They bring them in right away and say, "Look, we are going to develop this thingamajig. You need to go—how to figure out how to make it, and then—and put it in to your combat system and your tactics."

So you don't do—you have got to do it from the beginning, Congressman. That is the how you do it.

Mr. CRENSHAW. I appreciate your answer, and I have gone well over.

Thank you, Madam Chairwoman. I yield back.

Ms. ESHOO. The gentleman yields back. I am going to call on one more member, because she can't return when we resume the hearing—is the gentlewoman from Illinois, Ms. Kelly, and then we will break for the two votes.

And what time should we say we will be back, Mr. Brett?

VOICE. Mr. Brett?

Mr. GUTHRIE. Twenty minutes after the first vote—after the last vote.

Ms. ESHOO. OK, but how long is that? Just to give the witnesses an idea.

Well, why don't we—well, let's see what time we walk out, and then we will better estimate the time.

So the gentlewoman from Illinois, you have 5 minutes—

Ms. KELLY. Thank you so much, Madam Chair and Ranking Member Guthrie, for holding this hearing on ARPA-H.

It is well-established that our country faces large gaps in access to care, and that the color of your skin can determine the quality of your care and your health outcomes. Despite these inequities, Black and Latinx scientists who are well aware of the role these inequities play in their communities continue to be funded at low rates.

According to the NIH, in 2020 only two percent of funded NIH research project grant applications have Black or African American lead scientists, and five percent had Hispanic or Latinx-led scientists.

Ms. KROFAH, how can ARPA-H prevent repeating the mistakes of the past, and fund a diverse pool of researchers working across biomedical and community-based settings?

Ms. KROFAH. Well, thank you so much for your question. It is a problem. It is exactly a problem, just as you have stated. And what we need to do is to make sure that we don't repeat the mistakes of the past, which is a nice to have, but not a must have.

What we typically say is, "Write a community action plan, and send us your ideas of how you are going to do outreach," but there is no accountability in the end.

I think we have the opportunity to take all of the learnings that we have gone through to really put that into place with ARPA-H. We should have targets. We should say, "What are the diseases that are affecting the most number of people that are bearing the highest burden of disease, and how do we innovate there?"

We also need to make sure that we are hiring the right program managers from these diverse perspectives, and we need to set some

targets, and we need to have a patient advisory council that is diverse. I think those are issues that we just should not shortchange.

We should not broaden into language that is not specific enough that we do nothing about. So I completely agree with you. I think we can write that in to make sure it happens.

Ms. KELLY. So would you consider those to be metrics that would be used to determine if ARPA-H is funding a diverse pool of scientists, or are there other things you would suggest?

Ms. KROFAH. I do think that we need to make sure that we have metrics. Again, we do want to make sure that ARPA-H has the flexibility to pursue the science and the innovation, wherever that lies—of course, understanding that there is a public health need at the end of the day.

Outlining a strategic plan that includes metrics and it is transparent—what diseases, and why, for whom, to what benefit, and who are we bringing along—during those research studies needs to be clearly outlined.

And that also needs to occur in partnership with FDA, because a regulatory approval process happens there.

Ms. KELLY. As you know, some of the most successful and innovative interventions to improve health come from within impacted communities. For example, community health centers, hyperlocal healthcare hubs serving marginalized patients are often the epicenter of new ideas and cutting-edge innovation, from community-based emergency departments to trauma-informed behavioral healthcare.

How do you envision ARPA-H partnering with local communities to build upon the wealth of community-based knowledge that really already exists?

Ms. KROFAH. I think the program managers need to go out, and not rely on the communities to come in. We have these models. We use mobile clinics to go out into the communities. We need to do listening sessions. We need to take the managers and those messages out, wherever they are.

We can leverage platforms that were used to communicate around COVID-19 vaccination, turn those infrastructure into opportunities to listen to the communities.

But if we are going to stay in ivory towers with program managers who are all located centrally, and expecting those diverse communities to come to them, that just will not happen. So I do agree with you—

Ms. KELLY. Yes—

Ms. KROFAH [continuing]. And I do think those messages need to be taken out on the road, and to have those listening sessions with broad and diverse communities.

Dr. GIROIR. Ma'am, if you will, at DARPA my program managers in my office needed to be in the office two afternoons per month. I want to reinforce how important it is to get out into the communities. They are not going to be cooped up, they are not going to be in an ivory tower. They can't be behind walls. They have to go interact.

And the second point—and this is so important—is if you have an NIH system that ranks proposals 1 to 100, and only the top five get picked, you are going to lose all the diversity, because they are

not in the mainstream. They don't have the grantsmanship offices that Harvard or Yale or Hopkins do.

The whole goal of DARPA in the review process is maybe to take number one and three, but to pick that diverse approach, number 25 that is not from, you know, Harvard. And I am just using that stereotypically, but it might be from a community health center, or it might be from an HBCU. They would never make it to a traditional 1-to-end review process, but having that—diversity is a means to success. It is a goal in and of itself, but more than anything it is a means to success, particularly in the health realm.

Ms. KELLY. Well, thank you both so much. Thank you for your patience. Thank you for being witnesses, and I yield back.

Thank you, Madam Chair.

Ms. ESHOO. You are most welcome. I am glad we could accommodate you.

Ms. KELLY. Thank you.

Ms. ESHOO. All right. I think that—well, we are going to go over to vote. We will recess, and we are going to try to be back here by 2:20. All right?

And then, I don't know, I know I have two members from our side of the aisle, and a third that wishes to waive on. But we will make that determination when we come back.

Mr. GUTHRIE. Somebody can—

Ms. ESHOO. OK. Well, I am not—no one is going to be penalized if they come back.

Mr. GUTHRIE. I know—

Ms. ESHOO. They should be heard.

OK, the committee will recess until—

[Recess.]

Ms. ESHOO. The Subcommittee on Health will now come back to order.

The Chair is pleased to recognize the gentlewoman from California, Ms. Barragán, for your 5 minutes of questions.

Ms. BARRAGÁN. Thank you, Madam Chairwoman, for hosting this important hearing today. This bold proposal to create a new agency exclusively tasked to drive medical breakthroughs is so important because, among the 9,000 or so known human diseases, there are FDA-approved treatments for only about 500 of them.

To date, more than 146 drugs have been tested for Alzheimer's disease and rejected. While the first new drug for Alzheimer's in nearly 20 years was approved—recently approved by FDA, there is still a long way to go to truly treat and prevent the progression of Alzheimer's disease. ARPA-H has the opportunity to play a critical role in revolutionizing how we prevent, treat, and cure a range of diseases with unmet medical needs, like Alzheimer's, which affects millions of families across the country, including my own.

My first question is for you, Dr. Yamamoto. I am interested in how ARPA-H could help accelerate the discovery of Alzheimer's biomarkers as a means of tracking responses to potential Alzheimer's therapies and exploring the use of digital technologies for diagnosis, assessment, and disease monitoring, among other important research initiatives. Can you discuss how Congress can ensure there is transparency around ARPA activities, including data sharing and the open resources development of data and information?

Dr. YAMAMOTO. Thank you for that question, and let me start by saying that my dad died of Alzheimer's, so I know something about that from—at a very, very personal level.

Everyone knows that early diagnosis is probably the clearest route to being able to cure diseases, and neurological diseases are kind of the king of the failure to be able to diagnose early. My dad died when he was 84. In retrospect, I can think back to not quite a decade before that, but a number of—let's say, eight years before, when I could then, in retrospect, begin to think, oh yes, there was something going on, my dad. But we didn't know that.

But, in fact, right, there are things that are going on in the brain when the baby is born, or maybe before, right? We just don't know what they are. So the impact of being able to diagnose neurological disease early could go back to decades, seven decades. And think of the impact that we could have in being able to cure or prevent those diseases, if we knew what those early markers were. I think that ARPA has the capability—can develop the capabilities to be able to achieve such early diagnoses.

As we said before, when—what precision medicine does is collect enormous amounts of data about lots of people and experimental organisms, to be frank, that allow us to begin to pool that information, and begin to perceive biomarkers, indications of what the diseases are. So I can easily see an ARPA undertaking a project where at least the access to information to be able to establish those early markers is there to say that they have—a project manager could walk in and say, "I think the goal is that we want to diagnose Alzheimer's 15 years earlier than we can right now."

Ms. BARRAGÁN. Thank you, Dr.—

Dr. YAMAMOTO. I think we are beginning to pull together the data to be able to do that.

Ms. BARRAGÁN. Thank you.

Dr. Ling, part of the proposed mission of ARPA-H is to make pivotal investments in breakthrough technologies and broadly applicable platforms, capabilities, resources, and solutions that have the potentially—potential to transform important areas of medicine and health. This is a broad mission.

But what do you see as some of the greatest unmet needs facing human health, and how could ARPA-H help solve some of these unmet needs?

Dr. LING. Thank you, Congresswoman. I think that Dr. Yamamoto hit it right on the head.

One of the really ripe areas where a good period of investment could really make a big difference is the early diagnostics. And it is just not finding the widget that is going to identify the blood marker. It is also the analytical techniques that Dr. Yamamoto speaks of.

What does that mean? It means bringing in mathematicians and statisticians and physicists, potentially, into this discussion. It can't just be biologists and physicians. That is what an ARPA-H does. It brings in the people who are not commonly in the ecosystem into the ecosystem, bringing the chemists, bringing the entomologists, bringing the marine biologists, bringing—honestly no joke—the meteorologist, who looks at data at a large ecosystem-level, with the techniques that they do, to do something straight-

forward as weather. Apply those to the data sets that we are talking about right now.

You don't have to rediscover the wheel; you have to readapt the wheel. That is what an ARPA-H could do. It could bring in and create a new ecosystem, Congresswoman.

Ms. BARRAGAN. Well, thank you all for your responses. I didn't get to any of my other questions, but hopefully I will submit them.

Thank you, Madam Chairwoman, I yield back.

Ms. ESHOO. The gentlewoman yields back and now the Chair is pleased to recognize the gentlewoman from Delaware, Ms. Blunt Rochester, for your 5 minutes of questions.

Ms. BLUNT ROCHESTER. Thank you so much, Madam Chairwoman, and thank you to the witnesses for sharing your testimony today. I am pleased that we are discussing the Advanced Research Projects Agency for—

VOICE. Are you ready—

Ms. BLUNT ROCHESTER [continuing]. ARPA-H, which will accelerate the development of lifesaving treatments and cures in this country.

Last week the House passed the America COMPETES Act, a comprehensive package of—to bolster America's global economic competitiveness. And today we turn our attention to ensuring that the U.S. remains the leader in global biomedical innovation.

I am particularly interested in understanding how the interests of the American people can be protected, and how preventions and cures derived from the work of ARPA-H will be distributed equitably and ethically.

One of the goals of ARPA-H is to create platform technologies upon which others can build and innovate. Admiral Giroir, based on your previous experience with BARDA, how can the U.S. Government ensure that contractual agreements for the technology transfer and commercialization of products that use research sponsored by ARPA-H reflect the contributions of the American Government and the American people?

Dr. GIROIR. Yes, thank you for that question, and it is good to work with you again.

No. 1, the agency needs the flexible contracting authority to put that in. One cookie cutter does not fit. And as we heard, again, other transactions, cooperative agreements, all of those things.

No. 2, I would like to switch the paradigm a little bit. Instead of making sure that the next thing is distributed equitably, we ought—the next thing ought to be focused on equitable distribution as its primary goal, right?

So just as an early diagnostic could be, I could see a program that says we want to assure in the next five years that all the underserved communities have a projected life expectancy equivalent to those who are White and affluent. Now that is a big goal, but that is a DARPA hard goal. That is going to be prevention, preventing kidney disease, preventing hypertension, getting in the home.

So I think you have to design it from the start, not just do it as an afterthought.

Ms. BLUNT ROCHESTER. I love that, and it gets to the disparities issues that we have been talking about for years.

What guardrails could be put in place so that technology developed within the U.S. Government research funding is not exported for manufacturing overseas?

Dr. GIROIR. You know, that is not going to be necessarily the purview of ARPA, but I think it is very important.

Now, we talk about ARPA-H, you know, that the things that are going to be developed are going to benefit the world, just like the vaccines for COVID. America is, literally, saving the world. But we want to do our best to keep that technology here, so it supports jobs here, it supports the infrastructure here, that we don't get it copied by foreign—you know, overseas, that we don't get hacked, and all that gets done away. Again, these are all vital things.

And again, as Geoff said earlier, DARPA has been managing this. You know, things that are developed now won't necessarily be public for 30 years. The technology needs to be protected. I think we have the model. I think we have to employ the model and adapt the model, but I think your concerns are incredibly right on target, ma'am.

Ms. BLUNT ROCHESTER. Thank you. Thank you so much. And I am going to ask this question of the panel, and I will call you, and if I don't get to you, if you could submit it in writing, that would be great.

And how will we know if ARPA-H is successful, given the lag time between product development and commercialization?

And if we could, start with Dr. Yamamoto.

Dr. YAMAMOTO. So I think that we want to be able to look at the nature of the projects that are undertaken, and think about the scope, the breadth of application that—if the capability is developed. So we want things that don't focus on one disease, but things that will be effective for big clusters of them. I think that would be one measure that we could begin to apply to examining and evaluating the projects that ARPA-H comes forward with.

Ms. BLUNT ROCHESTER. Great, thank you.

And Ms. Krofah?

Ms. KROFAH. Yes, I would say understanding the impact on health outcomes through an ARPA-H program or intervention. Have we actually seen a difference in a disease or classes of disease states and, in particular to what Admiral Giroir just mentioned, equitably, across different populations who suffer disproportionately?

Ms. BLUNT ROCHESTER. Great, thank you.

And Dr. Ling?

[Pause.]

Ms. BLUNT ROCHESTER. Microphone.

Dr. LING. I think that there are metrics that we can use that are in existence. How many patents is one of them. The second is how many have transitioned into commercial practice. That is No. 2. No. 3 is how many have transitioned into clinical use and adopted by patients.

These are all metrics that have existed. DARPA, for example, has metrics looking at the dollars that are invested, and the return on investment in terms of commerce-produced, and it is a 10-to-1 ratio if you don't include the internet. If you include the internet, then it becomes, you know, astronomical.

So there are metrics that we can use that at all different levels that can actually be brought to bear to look at metrics of success—and failure, I might add.

Ms. BLUNT ROCHESTER. Yes, my time has expired. But Dr. Miller?

Dr. MILLER. Yes, I think we have to look at measures that are clinically relevant. So did we change how people practice medicine? Did we change how consumers access healthcare?

And then I think we also need to measure if that is distributed fairly and equitably because, frequently, it is not.

Ms. BLUNT ROCHESTER. Great, thank you so much.

Dr.—or Admiral Giroir, we will get back to you later.

And again, thank you so much, Madam Chairwoman, for this important hearing. I yield back.

Ms. ESHOO. Well, thank for your patience and for participating. Let's see who—oh, we have—

The Chair is pleased to recognize the gentlewoman from Massachusetts, Mrs. Trahan, for 5 minutes.

Mrs. TRAHAN. Well, thank you, Madam Chairwoman, and thank you to the witnesses here today. I am pleased that this subcommittee is holding important discussions on the establishment of ARPA-H.

Developing multiple vaccines within one year to effectively prevent serious illness and death from COVID-19 was unprecedented, and this outcome was made possible by significant Federal investment and collaboration with the private sector. Seeing what we accomplished in such a short time to save lives from COVID-19, it only makes sense for the numerous research projects out there to receive that same level of investment and urgency.

Those increased levels of investment and urgency is critical for people like my dad, who has been living with MS for 25 years, and who will benefit from the next innovation or lifesaving cure. However, barriers and gaps exist within the public and private biomedical research ecosystem, which can lead to the stalling or failure of innovative projects.

So to address this research gap, the Biden Administration has proposed the establishment of ARPA-H, and I am a big fan of the DARPA model, which ARPA-H will follow, including the groundbreaking discoveries we all know so well: internet, GPS—we could go on and on. So I am excited to witness the groundbreaking discoveries that will come out of ARPA-H.

Dr. Ling, how can we ensure the appropriate resources will be allocated toward high-potential projects?

Dr. LING. Again, it begins with the program managers and the construct of the agency itself. If we are following the DARPA model, which I totally advocate, completely and totally, what it is is that program managers develop the program that they think is appropriate.

Let's say, using Dr. Yamamoto's case, it is for a new analytical approach that could be applied broadly across a number of different diseases. That program manager will then construct the program. What are going to be the milestones? What, in fact, are going to be the performers staff? And then they ask for the money.

So the money isn't allocated initially. One program maybe gets \$10 million. Another program might get \$50 million, and another program might get \$100 million. It is dependent upon resourcing properly the program, and what the program hopes to achieve. As I said to you before, the most critical element is proper use of the dollars. And that is—it is the how. I always said it before, it is the—how the dollars are spent.

And so what you want to do is be sure to adequately resource the performers to achieve the goals of the program, as they are outlined from the get-go. The one thing you don't want to give them is time. Time is the one resource that we are not going to want to give to the performers. We will give them money, we will give them people, we will give them equipment, but not time.

Mrs. TRAHAN. I appreciate that.

Ms. KROFAH. I am wondering if you could just expound a little bit on how we can ensure that, you know, profit will not be the main driver for the development of a device, a treatment, or a technology, or a cure under ARPA-H.

Ms. KROFAH. Yes, thank you for that question. You know, what is the most important, as we think about these sets of challenges, is to go back to that patient perspective. Where are we seeing high burdens of disease? What are the issues that are affecting that high burden of disease? What is the role of technology? What is the role of analytics? What is the role of diagnostics? How do we address those sets of issues?

And then work backward from there to really address the science and the innovation question. Once we do that, that should yield the results that we are looking for. And that is why we make sure that we translate that science into what can be accessible for those patients at the end of the day.

It is not about the money, it is not about the profit motives at the end, because that is the issue why we are not seeing particular types of innovation targeted to patients who are suffering on the ground from diseases that we all know very well that we have not made a difference in decades and decades.

Mrs. TRAHAN. Great. And then, you know, my colleague from Delaware asked about metrics, and I think that is on all of our minds. How do we know if we are going to be successful?

I guess, once established, how long do you expect it to take to measure the success of the new agency through some of the metrics that were mentioned?

And I know that the clock is ticking down, so, Ms. Krofah, I will start with you.

Ms. KROFAH. I think metrics should start from day one. How quickly does the agency get up and running?

And then we should go and talk about how quickly do the program managers get established, and how quickly do those projects get funded and get started?

And then, of course, what kinds of science yields the outcomes over time? This could be a year, it could be 5, it could be ten years, but the metrics need to start on day one.

Mrs. TRAHAN. Great. Well, I appreciate you all being here. I look forward to working closely with the Administration and the important stakeholders as the ARPA-H proposal comes into fruition.

Thank you so much, I yield back.

Ms. ESHOO. Thank you. It is always enlightening to hear the questions that you pose.

Is Mrs. Fletcher with us? Is she poised to question?

Mrs. FLETCHER. Yes, Chairwoman Eshoo.

Ms. ESHOO. Oh, there you are.

Mrs. FLETCHER. Yes.

Ms. ESHOO. OK, I am pleased to recognize you, the gentlewoman from Texas, Congresswoman Fletcher, 5 minutes.

Mrs. FLETCHER. Thank you so much, Chairwoman Eshoo. Thank you for allowing me this time to participate in this hearing, and thank you for holding this hearing on the proposed creation of ARPA-H. I want to thank all of our witnesses for being here today, as well. This has been a really interesting and informative hearing.

And I know I have said before on this committee one of the reasons I was so excited to become a member of this subcommittee was because of its jurisdiction over medical research, and that is because of the community that I represent in Houston, Texas. I—my district lies just west of the Texas Medical Center, which is the largest medical center in the country. It employs more than 300,000 people, many of whom live in my district, including some of the researchers that have done this incredible research we have been talking about today.

I know Dr. Schrier was talking a little bit about CAR-T therapies earlier, and, of course, Dr. Jim Ellison, who won the Nobel Prize for his cancer research on this very issue lives in my district, and was my guest at the State of the Union two years ago. So I am just so proud to represent these incredibly creative, innovative, thoughtful, and really pioneering researchers in my district.

So I am very supportive of the ARPA-H proposal that is before us today. I am glad to have co-sponsored both Chairwoman Eshoo's bill, the ARPA-H Act, and Congresswoman DeGette's bill, the Cures 2.0 Act.

And as we have discussed throughout the hearing, the agency is modeled on DARPA, which has led to key innovations like GPS and the internet, things that we now couldn't imagine living without. And it could be that ARPA-H leads us to that next medical breakthrough that will revolutionize healthcare as we know it.

But there are key differences between DARPA and ARPA-H, and one of them that is really notable is that DARPA has, one, major customers that helps set its priorities, right? The Department of Defense. Whereas, when it comes to the biomedical ecosystem, there are various players, ranging from scientists to pharmaceutical companies to patients that are setting the agenda. And all these players have a crucial role in developing biomedical solutions that improve the lives of patients every day.

So I am interested in talking more about and learning about your thoughts on the role that ARPA-H will play within this larger system, and I want to direct my first question first to Ms. Krofah.

You discuss how ARPA-H must be engaged with other agencies. We have talked about that throughout the hearing, engaging with CMS and FDA. And you know, these things are critical to advancing solutions for patients. How do you envision ARPA-H working in a collaborative manner with these other agencies?

Ms. KROFAH. Thank you so much for the question. I mentioned in my written testimony and earlier this morning that I believe it is critically important that we have an advisory council and engagement with patients, engagement with industry, engagement with non-profits, engagement with academia to listen.

And of course, we need to listen throughout the country. We don't need to sit in the ivory tower, as I mentioned earlier before. I think that would be critically important to understand the kinds of issues that are motivating people to ask questions: What is holding back science for me, and why? And to bring forward their solutions to inform the program managers as they outline the proposals that they put forward to the ARPA-H director.

Mrs. FLETCHER. Terrific, thank you. You also mentioned in your testimony that the private sector will be an important partner for ARPA-H. Can you discuss—and I know we have touched on it throughout the day, but with the kind of minute-and-a-half I have left, there varying opinions here, and we have heard some of our colleagues on the other side of the aisle really want to defer more to the private sector. But can you discuss why it is so important for the private sector and other stakeholders to help work together to ensure that the project that ARPA-H supports ultimately lead to improvements in health for patients?

Ms. KROFAH. Yes, absolutely. The biomedical innovation is an ecosystem. It is not one actor. And each part of the ecosystem matters to all the other parts.

So when we talk about the totality that end-to-end solution set, as was outlined by some colleagues, we need R&D upstream to be connected downstream to where manufacturing occurs and, importantly, where those products end up going to patients. And that is really the role of the private sector. That last mile is an area where the private sector has significantly innovated the manufacturing capacity that we see.

Even when we got the COVID-19 vaccines over the finish line, we needed vast manufacturing capacity and capabilities in order for those vaccines to reach patients. And then the delivery points, right, the retail sites, the mobile clinics, outreach to the community settings. These are all the roles that we need to engage the private sector.

But also, importantly, they need to bring their expertise to bear. Many of these companies are also investing in different types of technologies. They can identify where the gaps are. Data analytics is a big gap. Our data ecosystem is quite siloed. We do not talk well to each other. If you are in one hospital setting, your data is not carried over to another hospital setting. If you are in one pharmacy, your data is not carried over to the other pharmacy.

How do we break down these barriers in data silos? The private sector can come forward and say, "We may not be able to solve it as one company," but we can put forward a project like ARPA-H, where it can break down those issues and those barriers.

Mrs. FLETCHER. That is terrific. Well, thank you so much. I see I have gone over my time, so I just want to thank you for that explanation, and really reminding us all about the ecosystem, and how we can accomplish so much when everyone works together.

So Chairwoman Eshoo, thank you so much for bringing us together for this hearing, and I yield back.

Ms. ESHOO. I thank the gentlewoman, and you should know that this big screen carries your beautiful face and voice. It is exciting, you know? We really get—with the screen you get a real close-up.

[Laughter.]

Ms. ESHOO. I am glad it is not of me, but it is wonderful to see colleagues on the big screen.

Now we welcome—we are grateful to Congresswoman Diana DeGette. She is not a member of our subcommittee, but she is waiving on, an important member of the Full Energy and Commerce Committee and one of the authors of Cures 1.0, now with 2.0.

And I want to reState my intent that ARPA-H and Cures 2.0, they are complementary, and the Chair will seek to move them together so that we could advance the legislation not only through the full committee, but the full House of Representatives, as it is so important that we do.

And with that, welcome, Diana, and you have 5 minutes.

Ms. DEGETTE. Thank you so much——

Ms. ESHOO. And if you go over a little, it is OK, we are just about done.

[Laughter.]

Ms. DEGETTE. OK, thank you. Thank you so much——

Ms. ESHOO. You have waited all day.

Ms. DEGETTE. I will just be happy to bat clean-up. Thank you so much, Madam Chair. Thanks for letting me waive on, although I do consider myself to be sort of an adjunct member of this subcommittee, anyway. And I want to thank you for your commitment to working with me and Congressman Upton on both this important initiative, ARPA-H, and also Cures 2.0, which really, really have synchronicity and need to go together.

When Fred and I first teamed up in 2015 to draft the 21st Century Cures bill, we couldn't have imagined the incredible success it would have for this country. And because of that Act, we have a better understanding of the human brain. We have made huge strides in regenerative medicine. We have increased funding for Alzheimer's research and cancer research. Congresswoman Trahan talked about Operation Warp Speed. Many people don't think we would have been able to get the vaccine that we did without the pathways that we had in 21st Century Cures. And, as Fred likes to say, it passed out of this committee 57 to 0. And of course, through the House and Senate.

And so I want to talk both about ARPA-H and Cures 2.0 today to hear how they can work together to have even more stunning advances in U.S. biomedical research. I would like to start with you, Ms. Krofah.

What are pathways and programs that were included in 21st Century Cures—or why are they, like the Moonshot and the Breakthrough Devices program, critical to the continued success of technological innovation?

Ms. KROFAH. Well, thank you so much, Congresswoman DeGette, and I very much applaud the efforts for Cures 2.0, and certainly your commitment to 21st Century Cures 1.0 that passed a number

of years ago that has had a tremendous impact on the biomedical innovation ecosystem.

You know, I will start by saying the role that patients have in providing their data toward medical research, contributing their data into the ecosystem, was supported through 21st Century Cures, and continues to be continue on the landscape. At the same time, seeking opportunity for breakthrough therapies and breakthrough designations has allowed us to see many new therapies reach the market to treat conditions like cancer, and many different types of cancer we would not have seen, otherwise.

And as we think about ARPA-H and the potential to merge the proposals that are in Cures 2.0, with an ARPA-H model, what it reminds me of is that close collaboration that is needed between ARPA-H and FDA, similar to what is in Cures 2.0, in terms of encouraging communication between FDA and—being able to bring that regulatory science up front at the time of determining the program or project is and creating that regulatory throughout that process will create clarity through the breakthrough process, will enable us, ultimately, to get the product create ARPA-H into products that are approved by FDA and, ultimately, to patients.

Ms. DEGETTE. Great. So what you are really saying is you see Cures 2.0 and ARPA-H as complementary, not substitutes for each other. Is that correct?

Ms. KROFAH. That is absolutely correct.

Ms. DEGETTE. And I—Dr. Yamamoto, I see you nodding your head yes. Do you agree?

Dr. YAMAMOTO. Absolutely, I agree. And I think the other—the thing I would add to what you just heard is that I think that—I said earlier that there is nothing in the Federal Government that incentivizes agencies with different focused missions to really cooperate and work together. And in many ways, Cures 2.0—and Cures 1.0, but also Cures 2.0—begins to do that. It doesn't—

Ms. DEGETTE. Thank you.

Dr. YAMAMOTO. It doesn't create the natural drive for collaboration that ARPA-H does, because that is what the—the only—the program managers know that the only way they are going to get there is to bring together different groups.

Ms. DEGETTE. Right.

Dr. YAMAMOTO. But—

Ms. DEGETTE. And Dr. Ling, I saw—I also saw you nodding your head. Do you agree with that?

Dr. LING. I fully agree with that. The ultimate goal here is to improve healthcare for everybody in this country, for every American citizen. And to do that you have to attack the entire problem in toto. ARPA-H is just a small piece. Cures 1.0, Cures 2.0, in fact, actually embrace much more of the health reform, the policy issues, working with FDA, and a number of other things that are absolutely essential to realizing this ultimate goal that we have.

Ms. DEGETTE. And Admiral Giroir, I can't see you, but I am hoping you were nodding your head, too. What is your view on that?

Dr. GIROIR. I actually could not agree more with you. These are not only complementary, but synergistic. They can't live without each other.

And I will just make one comment, as I do believe a significant minority of program managers at ARPA-H come from FDA or NIH, because they will have been frustrated at things they couldn't get done within their own agency, will come to ARPA to get it done, and then return richer and the country better for it.

Ms. DEGETTE. Great, thank you. Well, thank you to all of you for your leadership. I appreciate it.

Madam Chair, I just would like to take a moment of personal privilege on something else. One of our colleagues was attacking Dr. Fauci earlier, and calling him names.

And I want to say that, for Dr. Fauci, for all of our research scientists and our public servants who have worked hard to get us through this pandemic, including all of you, I want to say I appreciate what you are doing. I appreciate the advice and the science that you are relying on. And I want to apologize on behalf of the U.S. Congress that many of you have had to get security details because you have been under the threat of violence and worse. So thank you. Thank you to all of our advisors and scientists for getting through this. We will continue to do that.

And I yield back.

Ms. ESHOO. The gentlewoman yields back. I thank her for her—for not only her questions, but for—to recognize the extraordinary service of people: Dr. Fauci, so many others.

You know, I often think that those that are in the public sector, like he is, like so many are, they could be making millions of dollars a year in the private sector. Millions, tens of millions a year, a year. He devoted an entire lifetime to serve the American people. And you know, whether we agree with each other or not, to—that honorable servants of the people are attacked, that really has no place. That is not America. That just isn't America. So thank you for raising that.

I want to thank all the witnesses. I love hearings. I have to admit that. So if I sit here for 7 hours, the only regret is that my—or ranking member that I am dragging along with me, although he is a very, very attentive member—you have, I think, filled this room, whether you were—are with us virtually or in person, with very, very rich testimony, and very direct answers to our direct questions.

And so you have enlarged the issue that is before us. And your expertise, I think, whomever is listening in at home, that they would really be applauding the experts that we have in our country. And that you have come forward to advise the Congress is your gift to our country, and you have added immeasurably to our thinking today and helped us to improve the legislative vehicle that is before us. So on behalf of all of the members of the subcommittee, we all thank you and applaud you.

Now I need to get a—I request unanimous consent to enter the following documents into the record. Do you want me to read them?

Mr. GUTHRIE. No, no. No objection.

Ms. ESHOO. Oh, no objection? So ordered.

[The information appears at the conclusion of the hearing.]

Ms. ESHOO. They will be entered into the record.

That—our panel has completed their work today. And I think that you all deserve at least a martini this evening before dinner.

And Members have ten business days to submit additional questions for the record. So, to the witnesses, when we get those to you, please answer as promptly as you can to any of the questions that you receive. That is—it is not just appreciated, but it is an important weighing in, and we always want members' questions to be answered.

So with great gratitude, at this time the subcommittee is adjourned.

[Whereupon, at 2:58 p.m., the subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

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STATEMENT OF ERIC S. LANDER
Director
Office of Science and Technology Policy
Executive Office of the President

BEFORE THE

Subcommittee on Health
Committee on Energy and Commerce
U.S. House of Representatives

HEARING ON

ARPA-H: The Next Frontier of Biomedical Research

February 8, 2022

Good morning, Chairwoman Eshoo, Ranking Member Guthrie, and distinguished members of the Subcommittee. It is truly an honor to appear before you today, and I am grateful for the opportunity to discuss the Advanced Research Projects Agency for Health (ARPA-H)— an exciting new agency that the President has proposed to drive breakthrough advances in health and get them to patients quicker than ever before.

The Biden-Harris Administration is proposing ARPA-H because we stand at a remarkable time of scientific possibilities. The biological and biomedical sciences have made some remarkable advances over the last couple of decades. For example, we have learned how to train our own immune system to fight cancer and how to harness the power of cellular instructions, mRNA, to rapidly develop safe and

effective COVID-19 vaccines. And those are just a glimpse of the types of medical breakthroughs — from the molecular to the societal — that are possible.

Despite the progress, there is still tremendous need for medical breakthroughs. During the many listening sessions that OSTP and NIH hosted about ARPA-H, we heard powerful stories about individual patients with serious diseases — ranging from pediatric brain cancer and pancreatic cancer, to Parkinson’s and ALS, to a host of rare diseases — where, despite the medical advances in recent decades, breakthroughs are still desperately needed. There are many such stories among my own family and close friends, and I know there are many among yours as well.

We also need breakthroughs to address inequities in care, inequities experienced in rural areas, inequities experienced by communities of color, and inequities experienced by the disability community, among others.

The combination of human needs and remarkable possibilities challenges us to ask: *What more can we do to speed and revolutionize medicine — to lay the foundation — to improve the health of all Americans? And, how can we also drive innovations that transform healthcare access, equity, and quality, and reduce disparities?*

What might be possible? For example, one idea would be to use mRNA vaccines to teach our immune systems to recognize the 50 most common mutations in cells that drive cancers, so that our bodies would recognize and eliminate early cancer cells before they ever create a tumor. Another idea is to develop molecular ‘zip codes’ that would deliver drugs into only the specific types of cells where they are needed; this could greatly increase the efficacy of drugs and avoid side effects. But, transformative innovation can occur not only at the level of cells, but also across healthcare. A third idea would be to apply innovation to our Nation’s efforts to address health inequities across America, particularly in underserved and low-income communities. We could bring together community health workers and

cutting-edge health technologies to create effective systems that could help people manage chronic health conditions — with the goal of demonstrating rapid impact on health predictors, such as predictors of stroke and diabetes. We want to be able to encourage and to seize hundreds of ideas like these. ARPA-H can help us do that.

An important question to ask is: *Why do we need a new kind of research agency, ARPA-H, to drive this? Don't existing mechanisms suffice?*

The current biomedical research ecosystem in the United States is truly amazing. It consists of two components. The first is pathbreaking, curiosity-driven, *fundamental* research, largely supported by the National Institutes of Health (NIH), as well as other agencies, focused on understanding how the body works in health and disease; the NIH is recognized around the world as the crown jewel of biomedical research. The second is a vibrant biopharmaceutical industry focused on taking research through the development pipeline to bring vaccines, therapies, and devices to patients.

Unfortunately, the current system has gaps. Bold ideas that could make a big difference for patients can fall into these gaps, because they don't fit well within our mechanisms for supporting either fundamental research or commercial products. These ideas are often “use-driven” research — that is, research directed at solving a practical problem. They don't fit into existing mechanisms because they may be so risky, so costly, so broad in scope, so applied, so long-term, or so complex — in terms of requiring complex coordination across different groups— that they aren't suitable for basic research grants and also aren't suitable commercial projects.

Let me emphasize: The goal for ARPA-H is to fill an important gap. It's not to duplicate work that NIH already does. And, it's not to crowd out private sector efforts. The goal is to test transformative ideas that can have wider, faster impact than could happen through existing mechanisms — in the spirit of endeavors like the Human Genome Project or Operation Warp Speed.

Advancing these kinds of ideas requires a different approach to supporting biomedical research — one that exists in other areas of research and development — notably, at the Defense Advanced Research Projects Agency (DARPA).

As you know, DARPA is the legendary Defense Department agency that laid critical groundwork for the Internet, GPS, and much more. Launched in the wake of Sputnik, DARPA's mission is clear — to make pivotal investments in breakthrough technologies for national security. And it has been successful by pioneering a model that smartly blends boldness with discipline. For example:

- DARPA aims to be a lean and nimble organization with a fair amount of autonomy. It focuses on mission-driven research that could offer extraordinary returns, and program managers are empowered to take on bold, transformative ideas.
- At the same time, DARPA also brings discipline, including by placing limits on a program's duration and on staff's tenure. Program managers are appointed to short terms — typically around 4 years. Its director also serves for a limited period.

ARPA-H proposes to apply a similar model to propel bold projects in the biomedical and health ecosystem. The President's vision is to create a new kind of entity for biomedical research that will have the autonomy, authorities, and resources to boldly tackle big challenges facing human health. It will aim to benefit the health of *all* Americans by catalyzing health breakthroughs that cannot readily be accomplished through traditional research or commercial activity. It will support transformative programs that enable the emergence of new technologies, new capabilities, and new platforms to drive progress — across a broad range of diseases.

In doing so, programs supported by ARPA-H will focus on practical solutions through use-driven research that aims to foster breakthroughs ranging from the molecular to the societal scale — including advancing both individual health and health equity for all Americans. Because equity will be an essential

element of ARPA-H, it will be key to its practices, including in hiring program managers with diverse perspectives about health challenges, in selecting programs that aim to fulfill a diverse range of needs, and in building interdisciplinary teams with unique expertise to accomplish program goals.

Echoing many elements of the DARPA model, ARPA-H will embrace urgency, nimbleness, and innovation, while also ensuring discipline. To do that, ARPA-H's culture will be key to its success. Like DARPA, it will have a flat, dynamic organizational structure — and the director and program managers will serve for only a limited time.

ARPA-H program managers will be given broad autonomy and the authority to drive innovation and be creative with their programs. They will each bring ideas about areas that are important and ripe for progress, and they will then solicit bold proposals in these areas. Adopting the DARPA model for review, ARPA-H program managers will use expert reviewers to evaluate whether the proposals hold great promise and meet the needs of the program, and then they will have the authority to assemble portfolios of projects and teams to tackle important goals. Through this model, DARPA attracts remarkable people to come into the federal government for limited periods of time to try to make a big impact; ARPA-H will aim to do the same.

We should be clear: Some ARPA-H programs will fail. That's not only OK — it's an essential feature of the model. To take on potentially transformative ideas, one must accept some degree of failure. If no ARPA-H programs fail, then ARPA-H is being too risk-averse.

ARPA-H will need to work across a wide range of sectors, including having close relationships and collaborations with patient groups, industry, academia, NIH Institutes and Centers, and other federal agencies. It will also need to work across a wide range of disciplines, including those that don't traditionally engage in biomedical research, to draw them in. ARPA-H should avoid areas of research that are already well-supported by research stakeholders, unless it can bring a very different approach.

In addition to having a distinctive culture, ARPA-H needs flexibility—for example, concerning how it hires program managers, how it reviews proposals, and how it makes funding decisions. And, it's critical that the ARPA-H director have complete independence and autonomy with respect to scientific direction and program selection.

We look forward to working with the Congress on how best to design ARPA-H, because I know we all want to get it right.

In summary, I believe that ARPA-H has the potential to revolutionize how we prevent, treat, and cure a range of diseases that impact Americans' health and quality of life. The DARPA model is not the right approach for all challenges, but it's a powerful approach for driving certain kinds of innovation — including the kind of innovation we need for health, transforming the seemingly impossible into reality.

Matthew Might, a patient advocate and computer scientist who lost his son Bertrand to an ultra rare disease, put it like this, "For all lives lost for failing to move as swiftly as possible, establishing ARPA-H honors their memory." The time to act is now.

Thank you Chairwoman Eshoo, Ranking Member Guthrie, and all the Members of the Subcommittee for your consideration of this critical issue. I look forward to addressing your questions.

SEPTEMBER 8, 2021

To: The Honorable Joseph Biden
President of the United States

The Honorable Xavier Becerra
Secretary of Health and Human Services

The Honorable Nancy Pelosi
Speaker

The Honorable Kevin McCarthy
House Republican Leader

The Honorable Chuck Schumer
Senate Majority Leader

The Honorable Mitch McConnell
Senate Republican Leader

Dear President Biden, Secretary Becerra, Speaker Pelosi, Majority Leader Schumer, Leader McCarthy, Leader McConnell, America's Lawmakers, Patient Advocates, and Fellow Americans:

We lead, fund, and count on the many small biotechnology companies that develop medicines for diseases* that lack sufficient treatments and cause considerable suffering. The companies led by the executives among us employ 23,250 people in the US and collectively invest over \$17.7 billion/year in search of breakthroughs. We are currently testing 407 new and potentially life changing drug candidates in clinical trials, some of which build upon foundational NIH-funded research led by the academic researchers among us. The investors among us work at firms managing over \$185 billion of life science-focused capital that comes primarily from pension funds, families, universities, non-profits, and others who invest in drug development. Many of us are also patients and patient advocates, with loved ones who suffer from difficult diseases in need of better treatment options. We have dedicated ourselves to that effort.

Collectively we come together to defeat disease. Each drug in development is a complex, time consuming, and expensive scientific and medical undertaking. Most of the time we lose the battle. But we persist because the few projects that succeed will forever improve human health.

Our industry invests over \$160 billion in R&D each year. In the past decade it has created vaccines and treatments for Covid-19, treatments for cystic fibrosis and sickle cell disease, and cures for several cancers and hepatitis C. These successes are just a few examples of the many significant advances we are driving. Our efforts are reducing the burden and threat of diseases across the USA and around the globe.

It has become clear that we must also help our lawmakers understand the basic economic framework that inspires companies and investors to take the financial risk required to create new medicines. Called to action by the justifiable outrage of patients who cannot afford their out-of-pocket costs, some lawmakers have misdiagnosed the problem. They believe drug companies charge too much for their products. In response, they are proposing to enact laws that not only fall short of making drugs affordable to all patients but also defund our efforts to create better ones.

To join us in signing this letter, [please click here](#) and you'll be asked to enter your Name, Affiliation, City, State.
We update this letter with signatories periodically, so your name won't show up right away.

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The Right Goal

To be clear, we are concerned about the high and rising out-of-pocket costs that have made our medicines increasingly unaffordable to many patients. We, too, call for a solution to affordability. We don't invent drugs to have them placed out of the reach of people who need them.

Insurance makes it possible for Americans to afford today's medicines and collectively invest in tomorrow's, as is captured in [this short video](#). To solve the problem of affordability for patients, we must lower the amount that insurance plans can make patients pay out-of-pocket, redefining proper insurance by law, just as policymakers have appropriately outlawed discrimination on the basis of pre-existing conditions.

The Wrong Policy

Instead, Congress is considering allowing the government to dictate the price that a company may charge for a novel drug with the threat of ruining the company financially with a 95% tax should the company refuse to accept the government's price.

Such draconian measures would immediately halt private funding of drug discovery and development. As an industry, we would no longer be able to infer what insurance plans might value and pay tomorrow from what they value and pay today, which is the premise of a market economy. Unpredictable government-dictated prices would supplant the current market-based framework that inspires biomedical R&D investment.

The investors among us would have to shift our investments toward areas still governed by markets, such as technology and consumer goods. Those companies with drug candidates in development would fail to raise more capital, making it pointless for them to spend existing dollars on ongoing research. The loss of hundreds of thousands of well-paying jobs would be swift, though it may take longer for the public to sense the loss of future treatments and cures.

Some may think NIH funding will be sufficient to fund continued R&D. The NIH is a crucial funder of the basic research that provides the ideas for what kinds of drugs might be possible.

Translating those ideas into actual medicines is almost entirely driven by the private sector and makes all that basic research worth funding in the first place. Some of us signing this letter are NIH funded academic researchers whose discoveries have had significant patient impact, and we affirm that the private sector has been and will continue to be essential for turning our ideas into medicines. The NIH and industry are parts [of one whole ecosystem](#), not a replacement for one another.

What's in a Word?

Successful negotiations result in market-based prices based on competing alternatives – this negotiation already takes place between drug manufacturers and insurance companies, resulting in an average 50% reduction from drugs' list prices to their net prices.

True negotiation requires that both parties can walk away from the table. True negotiation is acceptable to all of us and spurs us to compete. True negotiation means that even if we don't get to the market first, our second and third place drugs can still secure some market share by competing on price.

The proposed introduction of a 95% tax penalty would allow The Center for Medicare and Medicaid Services (CMS) to simply dictate any drug's price. This is not true negotiation.

As proposed, the government would be able to keep a company from walking away from an unacceptably low price. This gives the American public the impression that they can have any drug that's been invented for any price, however low. Overlooked in that bargain is that investors and companies will stop investing in new programs, and we'll give up the medicines that haven't been invented yet.

Congress may not intend to dictate the price for every drug. But dictating the price of drugs covered by Medicare would defund R&D for diseases of aging, including Alzheimer's, osteoporosis, and cancer. Dictating prices for medicines priced above a certain threshold would defund R&D for rare diseases. Dictating prices for medicines that generate the most total revenue would defund R&D for our most difficult diseases, since those are the ones that require greater expected revenues to incentivize substantial R&D investment.

Dictating prices for drugs deemed less "valuable" to society sounds tempting, until one realizes that the math for estimating a drug's value is so nascent, imprecise, and controversial that it's easily biased to reflect the preferences of the practitioner. For example, a recent business plan competition demonstrated that [not a single project would be fundable](#) if future products could only be priced in accordance with the [over-simplified math](#) used in the UK and Canada. Furthermore, there is mounting evidence from health economics research that medicines offer greater societal value than is reflected by their prices.

Better Solutions

We already have a functioning mechanism to drive down drug prices: drugs go generic. Because drugs go generic, what America spends on drugs has remained at roughly 10% of healthcare spending for decades, yet we have so many more effective and safer medicines today than in the 1970s.

Hospitals, long-term care facilities, and medical procedures do not go generic; those costs have only been climbing. We can keep ourselves from having to rely as much on hospitals in the future by inventing better medicines, which will then go generic. Society saves money, and we all lead healthier lives.

Preserving market-based incentives for drug R&D is how we get the medicines to achieve this goal. Heart transplants were first performed in 1967 and climbed in price by over 2,000% to cost \$1.4 million today. The heart failure drug amiloride helps avert the need for transplants and was approved in 1967; today it costs 26 cents/pill. We haven't solved heart failure, but we're working on it. So, there's hope for the people who need better heart failure medicines, but that hope requires continued investment in R&D.

America, and specifically CMS, can still save on drugs without sacrificing future treatments, cures, and vaccines. Certain drugs do not go generic even after their patents have expired, and CMS could save money by solving that particular market failure. Doing so would not reduce R&D incentives. [Members of industry](#) and others have proposed [a specific, actionable framework](#) for how this could work.

Averting A Costly Error

It's true that replacing market-based pricing with non-market government-dictated prices will reduce healthcare spending in the short run (the Congressional Budget Office, which helps lawmakers determine what legislation may cost or save the government, uses a 10-year timeframe). But without new medicines, this policy will condemn America to spend far more on managing diseases in hospitals and long-term care facilities for decades to come.

The worst part is that it will take a long time to realize that we're not making progress like we used to. For example, antibiotic R&D has historically suffered from low investment incentives because the prices of antibiotics are so low. Today, we urgently need new antibiotics to combat the rise of resistant bacterial infections, but it will take years to remedy this gap in R&D even with proper incentives and funding. It's hard to appreciate what we don't have until we need it.

The advocates among us know this acutely, having worked with so many patients struggling to make it to the next breakthrough.

Where there are market failures, we should fix them. All drugs should go generic without undue delay. Americans should not suffer because their insurance burdens them with unaffordable out-of-pocket costs, whether they get their drugs through Medicare, their employer insurance, or on the public exchanges. Patients and policyholders should benefit from the savings insurers negotiate with drug companies, and drugs covered under Medicare Part B should be subject to the same competitive

market forces as those covered by Part D. Lawmakers should focus on these important, achievable, and bipartisan reforms for the benefit of all Americans.

In the meantime, the term “negotiation” must not be redefined to encompass the government dictating a price under threat of financial ruin. Were such a law to pass, capital would be immediately redirected away from biomedical R&D, with an immediate effect on biotechnology jobs and longer-term harm to patients and our national budget and security.

Some observers of the drug development ecosystem who propose different theories and models of how it works might contradict us. But the executives and investors among us write not as observers of biotech’s economic framework but as its actual elements and conductors; capital and incentives flow through our funds and our companies like electricity through a circuit. It is evident to us that replacing true negotiation with dictated prices would defund R&D, like flipping off a light switch.

Sincerely,

Peter Kolchinsky, Aoife Brennan, Alex Karnal, Jeremy Levin, Laura Shawver, Daphne Zohar, and Signatories to this Statement, listed below**:

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ADHD, ALS, Alzheimer's, Amyloid diseases, Anemia, ARDS, Autism, Autoimmune Disorders, Benign Prostatic Hyperplasia, Blindness, Breast Cancer, Chemotherapy Induced Peripheral Neuropathy and Chemotherapy Induced Cognitive Impairment, Chronic Hepatitis B, Chronic Lymphocytic Leukemia, Chronic Pain, Cognitive Injuries, Colorectal Cancer, Complement Disorders, COVID, Dementia, DM1, DMD, Enteric Hyperoxaluria, Fragile X syndrome, FSGS, FSHD, Gout, Heart Failure, Huntington's Diseases, Idiopathic Pulmonary Fibrosis, IgA nephropathy, Infectious Disease, Inflammatory Bowel Disease, Influenza, Long COVID, Lung Cancer, Lupus, Major Depressive Disorder, Melanoma, MLD, MPS2, Multiple Sclerosis, NASH, NMOSD, Non-Hodgkin Lymphoma, Obesity, Opioid Use Disorder, Osteoarthritis, Ovarian Cancer, Pancreatic Cancer, Parkinson's Disease, Parkinson's Psychosis, Pediatric Leukemias, Pediatric low grade glioma, PKU, Post-surgical Pain, Primary Biliary Cholangitis, Prostate Cancer, Pulmonary Arterial Hypertension, Rare Epilepsies, Renal Cancer, Retinal eye diseases, Rhett's Syndrome, Stroke, Type 1 Diabetes, Type 2 Diabetes, Uterine Cancer, and many other diseases.

***The appended signatures do not necessarily reflect the policy or position of any agency, organization, employer, or company with which the signatories are affiliated.*

CC: House Energy and Commerce Committee Chair Pallone and Ranking Member McMorris Rodgers
House Ways and Means Committee Chair Neal and Ranking Member Brady
Senate Finance Chair Wyden and Ranking Member Crapo
Senate Health, Education, Labor, and Pensions Chair Murray and Ranking Member Burr

To join us in signing this letter, [please click here](#) and you'll be asked to enter your Name, Affiliation, City, State. We update this letter with signatories periodically, so your name won't show up right away.

STATEMENT OF THE NATIONAL KIDNEY FOUNDATION
30 EAST 33RD STREET NEW YORK, NY 10016
SUBMITTED TO THE HOUSE COMMITTEE ON ENERGY AND COMMERCE
SUBCOMMITTEE ON HEALTH
HEARING ON "ARPA-H: THE NEXT FRONTIER OF BIOMEDICAL RESEARCH"
SUBMITTED BY SHARON PEARCE
SENIOR VICE PRESIDENT, GOVERNMENT RELATIONS

February 8, 2022

The National Kidney Foundation (NKF) is pleased to offer the following comments and recommendations on the Advanced Research Projects Agency for Health (ARPA-H). The National Kidney Foundation is largest, most comprehensive and longstanding, patient-centric organization dedicated to the awareness, prevention, and treatment of kidney disease in the U.S. In addition, NKF has provided evidence-based clinical practice guidelines for all stages of chronic kidney disease (CKD), including transplantation, since 1997 through the Kidney Disease Outcomes Quality Initiative (KDOQI).

As it creates the policy and authority of ARPA-H, we encourage Congress to prioritize chronic kidney disease as an area for significant focus and investment. Despite the toll of chronic kidney disease (CKD) on patients, families, and society (including a disproportionate share of Medicare expenditures for individuals with end stage kidney disease), innovation in kidney disease research lags far behind that of other major diseases. The federal government's current support of kidney research funding is insufficient to meet this growing burden. An estimated 37 million Americans have CKD, but insufficient funding results in lost opportunities to slow disease progression, improve patient quality of life and potentially reduce expenditures by Medicare, Medicaid, and other public and private payers. Even treatment options for ESKD are identical to what they were 40 years ago: dialysis, transplant, or palliative care and hospice care.

CKD is a comorbid condition with other diseases such as diabetes, hypertension, and heart disease. Approximately 40% of individuals with CKD have diabetes, 32% have hypertension, and 40% have self-reported cardiovascular disease. ARPA-H can provide avenues for interdisciplinary research on devastating comorbidities.

Diagnosis, disease progression, home dialysis utilization, access to kidney transplantation, and kidney transplant outcomes differ greatly by race and ethnicity. Differences in CKD outcomes—

whether due to genetic factors, economic and social factors, or systemic racism—are unconscionable. African Americans, Hispanics, Asian Americans, Pacific Islanders, Native Americans, or Alaska Natives are at higher risk of CKD and ESKD than White Americans. African American and Hispanic populations experience more rapid decline of kidney function than non-Hispanic Whites. African Americans make up about 13 percent of the general population, but account for 35 percent of Americans with kidney failure, and Hispanics or Latinos are 1.3 times more likely than non-Hispanic or non-Latino people to have kidney failure. African Americans and Hispanics are also less likely to receive a kidney transplant. African Americans made up one-third of patients on the kidney wait list in 2019, but they received only 21% of transplants.

To address the dire need for additional kidney research and capitalize on scientific opportunities, NKF convened two Research Roundtables in December 2020 comprised of nephrology leaders from prominent academic institutions, the pharmaceutical industry, and other experts, to identify and prioritize opportunities for pre-clinical and clinical kidney-related research. An Advisory Group consisting of patients, transplant recipients, family members, caregivers, and living donors also shared their perspectives on areas in need of further study.

The resulting Roundtables Roadmap consists of more than twenty recommendations in pre-clinical and clinical research (including implementation science) where additional funding could help bridge existing deficits in CKD management and treatments, reduce incidence and progression, reduce health disparities, improve patients' quality of life, and potentially reduce Medicare expenditures. While the Roundtables focus was on NIH, we believe unique opportunities will be present under ARPA-H that can speed the identification and delivery of unique solutions that are not possible under the traditional NIH framework. We urge the leadership of ARPA-H to consider many of the priorities identified in this roadmap, including:

- Research focused on racial and ethnically diverse populations to better understand genetic determinants of health in a broad range of chronic diseases, including CKD.
- Grants for targeted systems for the delivery of therapeutic compounds to specific cell types.
- The development of new biomarkers that more accurately assess kidney function, disease progression, and disease management efficacy.
- Creation of a nationwide, integrated informatics infrastructure platform for kidney research in which datasets can be shared across institutions to facilitate new research opportunities and treatment advances.
- Development of clinical trial consortiums to recruit CKD patients to test potential high-reward research for assessment of kidney outcomes and increase the enrollment of underrepresented populations.
- Demonstration projects that focus on underrepresented populations, including individuals who are marginalized because of social determinants of health. Clinical interventions

with primary care teams, nephrology care teams, and community organizations can identify at-risk individuals and implement culturally appropriate cost-effective interventions to prevent CKD incidence, slow CKD progression, and reduce incidence of kidney failure.

Testing and implementing strategies to increase utilization of known therapies, especially in areas where cultural, community and other barriers inhibit access to treatment breakthroughs for marginalized populations.

Conclusion

We strongly encourage Congress to prioritize chronic kidney disease as an area for significant focus and investment as it builds out the structure and priorities of ARPA-H. Chronic kidney disease places a tremendous toll on patients, families, and our health care system, yet the level of kidney disease research in the U.S. remains inadequate. We have identified key areas in which additional funding could help bridge deficits in kidney disease detection and treatments and improve patients' quality of life while potentially reducing kidney-related health care costs. The Administration's ARPA-H initiative will provide the opportunity to test solutions for many of the priorities contained in our research roadmap.

Thank you for your consideration.

Beyond Diversity — Time for New Models of Health

Jane L. Delgado, Ph.D.

Despite the ability to collect and analyze far richer health data than ever before, public health and medical experts have failed to use that information to develop new conceptual models for health. Although data from research inform clinical decision making, many possibilities suggested by health data are lost when we insist on fitting those data into our existing health constructs rather than building new constructs on their basis. The

challenge is to ensure that the full range of what we know — from genomics to the social determinants of health for each person — is available, valued, and understood, which may necessitate the development of new models of health and illness. But though the accumulation of new evidence may warrant a paradigm shift, the human tendency is to hold on to our familiar conceptual models even when new data urge us to develop alternative ones.

Health data for Hispanic or Latinx people, who account for nearly one fifth of the U.S. population, provide a platform for re-conceptualizing health and risk factors. Contrary to expectations, Hispanic people with many known health risk factors (low income, low educational levels, lack of health insurance, diabetes, and excess weight) live longer than non-Hispanic White people in the United States; have higher rates of diabetes but lower rates

of cardiovascular disease; and even with low incomes and lower-quality prenatal care, have infant mortality rates only slightly higher than those among their non-Hispanic White counterparts. The health profile of Hispanic Americans does not adhere to the paradigm in which minority ethnic or poverty status determines poor health outcomes.

Instead of using Hispanic Americans' health data to recalibrate or rethink existing models of health and risk factors, however, the U.S. health enterprise has typically diminished the importance of the data on longevity and good health outcomes. Some health experts began referring to these findings as “the Hispanic paradox”¹ — the exception to the rule. As data from other countries in the Americas were revealed as supporting U.S. observations regarding longevity among Hispanic people, researchers responded not by developing a new model but by expanding the Hispanic paradox into “the Latin American paradox.”² Other researchers developed various explanations for longevity in Hispanic populations: the “salmon bias,” according to which Hispanic Americans did not in fact live longer but rather, like salmon, returned to their location of birth to die and were thus excluded from U.S. mortality data³; the hypothesis that only relatively healthy people migrated from Latin American countries to the United States; or the possibility that death certificates were being filled out incorrectly. The first two explanations were rejected in 1999, and in 2010 researchers put the third to rest.⁴ Yet even now, some observers dismiss the accuracy of outcome data for

Hispanic Americans, arguing that this population is too diverse to be analyzed as a single group — while overlooking the fact that non-Hispanic White Americans, Asian Americans, and African Americans are also ethnically diverse.

The opportunity that data for Hispanic populations presented for developing new models of health was ignored; analysts simply noted that the findings did not fit the prevailing conceptual framework for health, and there was no alternative model available to explain them. But unbiased analysis of data on the health of Hispanic and other communities can move us beyond existing conceptual frameworks and allow us to leverage modern science in elucidating mechanisms of health and disease. Achieving such progress will require several steps.

The first requirement is introspection and discernment. Data are neither collected nor analyzed in a vacuum. Though objectivity is assumed, what we measure is often affected by the prevailing culture. Cultural beliefs and values become lenses through which researchers and clinicians experience the world, and they often harden into biases that act as intellectual blinders. To look at information and data in a new way, researchers and clinicians need to acknowledge the influence of their own culture as well as their views of other cultures. Introspection is essential for identifying implicit beliefs and biases that become ingrained in research, models of care, and the artificial intelligence that increasingly both drives and undermines clinical decision making.

Second, we need to reconsider the value of decades-long trend

lines. If we focus only on areas of health in which we have sufficient data to produce trend lines spanning decades, we systematically omit substantial portions of the population whose data were not collected, and we remain wedded to health models that fail to reflect the realities of the current U.S. population. Though the national model death certificate includes the decedent's gender, race, and age, and has incorporated a Hispanic identifier since 1989, other sources of health information have included minimal Hispanic data (e.g., <6% in clinical trials, 3% in the Cancer Genome Atlas, and <1% in genome-wide association studies). The health data we are collecting — through the U.S. Census Bureau, Centers for Disease Control and Prevention, and Amazon — from the 24 million Asian Americans, 47 million African Americans, 62 million Hispanic Americans, and many other communities (American Indians, Alaska Natives, Native Hawaiians, Pacific Islanders, and others) no doubt carry important implications for future health and health care.

Third, it is important to collect data on multiple factors and to engage experts from varied disciplines — public health, medicine, economics, behavioral science — in analyzing those data. Building research enterprises (e.g., the National Institutes of Health “All of Us” research program) that aggregate multiple sources of data from varied disciplines, as well as using information gathered by commercial entities (from insurers to Meta [formerly Facebook]), can be part of the solution. These strategies can lead to new partner-

ships for the public health community and the availability of more data from diverse sources to help elucidate individual patients' health. Increased access to relevant data will allow for the aggregation (of data on everyone who identifies as Hispanic) and disaggregation (by specific ancestry) that can reveal the nuances of health risk factors in various racial, ethnic, or gender-based subgroups. Clustering diverse groups under a single category — “disadvantaged,” “minority,” “people of color,” “underrepresented minorities,” or “BIPOC” (Black, Indigenous, and people of color) — is not informative, since it homogenizes disparate health experiences. Moreover, other key aspects of human identity — such as gender, sexual orientation, religion, and disability status — also affect health. An appropriate model of health would include multiple factors in explaining, for example, why the leading causes of death among non-Hispanic Black Americans and non-

Hispanic White Americans are diseases of the heart, whereas those among Asian Americans and Hispanic Americans are malignant neoplasms.⁵

Fundamentally, it is not adequate to collect and analyze data from diverse people and sources. We must be willing to step back and look critically at what we think we know, reflect on the adequacy of current models, and pursue alternative models. The health effects of toxic substances in the environment, one's microbiome, and epigenetic factors can contribute to new paradigms. Researchers and clinicians who are open to more nuanced models that take into account multiple factors will be able to pursue an exciting new path.

Although many relevant fields are still in their infancy, in the future our understanding of health will be personalized and based on models that combine research findings in genomics and biology (the microbiome, immunology, and other areas) with compre-

hensive or integrative modeling built on public and private data sets. Without a fundamental shift in our conceptual models of health research and care, we will perpetuate the barriers we claim to want to dismantle and compromise the health of all communities.

Disclosure forms provided by the author are available at NEJM.org.

From the National Alliance for Hispanic Health, Washington, DC.

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Alzheimer's Association and Alzheimer's Impact Movement Statement for the Record

**United States House Committee on Energy and Commerce, Health Subcommittee
Hearing on "ARPA-H: The Next Frontier of Biomedical Research"**

February 8, 2022

The Alzheimer's Association and Alzheimer's Impact Movement (AIM) appreciate the opportunity to submit this statement for the record for the House Committee on Energy and Commerce, Health Subcommittee hearing on "ARPA-H: The Next Frontier of Biomedical Research." The Association and AIM thank the Subcommittee for its continued leadership on issues important to the millions of people living with Alzheimer's and other dementia and their caregivers. This statement provides an overview of how ARPA-H can play an important role in revolutionizing how we prevent, treat, and cure diseases like Alzheimer's, which affects millions of families across the country.

The Alzheimer's Association is the world's leading voluntary health organization in Alzheimer's care, support, and research. It is the nonprofit with the highest impact in Alzheimer's research worldwide and is committed to accelerating research toward methods of treatment, prevention, and, ultimately, a cure. AIM is the advocacy affiliate of the Alzheimer's Association, working in strategic partnership to make Alzheimer's a national priority. Together, the Alzheimer's Association and AIM advocate for policies to fight Alzheimer's disease, including increased investment in research, improved care and support, and development of approaches to reduce the risk of developing dementia.

Alzheimer's Impact on American Families and the Economy

Alzheimer's is a progressive and fatal brain disorder that damages and eventually destroys brain cells, leading to a loss of memory, thinking, and other brain functions. There are no survivors.

Alzheimer's is emotionally, physically and financially draining for individuals and families. In addition, Alzheimer's is creating an enormous strain on the health care system, and federal and state budgets. The annual cost for caring for individuals living with Alzheimer's or other dementia will total \$355 billion including health care, long-term care, and hospice care in 2021. The U.S. taxpayer-funded federal health care programs Medicare and Medicaid are expected to cover \$239 billion, or 67 percent, of these costs this year. In addition, American families provide an estimated \$250 billion in unpaid care. While an estimated 6.2 million Americans age 65 and older are currently living with Alzheimer's, nearly 13 million Americans will have Alzheimer's by 2050 and costs will exceed \$1.1 trillion (in 2021 dollars). Alzheimer's and other dementia threaten to bankrupt families, businesses, and our health care system.

Advanced Research Projects Agency for Health

The Alzheimer's Association and AIM support Congressional efforts to establish the Advanced Research Projects Agency for Health (ARPA-H). We are glad to see Alzheimer's listed as one of the disease areas of focus. However, we urge Congress to ensure ARPA-H does not duplicate or supplant current Alzheimer's research efforts at NIH. There are still many important unfunded targets that NIH can and should fund, as outlined in the [NIH Professional Judgment Budget for Alzheimer's Disease and Related Dementias for Fiscal Year 2023](#). One example of this great work is the Accelerating Medicines Partnership Alzheimer's Disease (AMP AD). The AMP AD program is a precompetitive partnership among government, industry, and nonprofit organizations that focuses on discovering novel, clinically relevant therapeutic targets and on developing biomarkers to help validate existing therapeutic targets. AMP AD 2.0 launched in February 2021, with the goal of enabling a precision medicine approach to the discovery of novel targets and biomarkers.

ARPA-H can fill an important role in supplementing the current work at NIH by driving transformational innovation in research and speeding the application and implementation of cutting edge breakthroughs. Examples of Alzheimer's-related projects ARPA-H could undertake are accelerating the discovery of brain imaging, eye imaging and blood or fluid biomarkers capable of measuring synaptic loss, neuronal death, and glial inflammatory pathways, as a means of tracking responses to potential Alzheimer's disease therapies. There are also opportunities to explore the use of digital technologies for diagnosis, assessment and disease monitoring, such as novel ways to measure and evaluate cognition and function of an individual, develop tools focused on voice recognition and other passive ways to measure changes that may be reflective of brain diseases, such as Alzheimer's. In addition, opportunities that will enable the complex modeling of contributions to risk are additional areas ripe for investment; such opportunities may help develop risk assessments based on the individual - including genetic, biologic, and clinical measures. We also urge ARPA-H to focus on activities that include providing a validated algorithm for disease risk using all available data, like biomarker, digital and emerging technology, to support a translatable resource for clinicians and drug discovery experts.

We caution that ARPA-H should not operate in silos or in isolation. Transparency surrounding the activities at ARPA-H will be key, as will data sharing and the open resources development of data and information.

Conclusion

The Alzheimer's Association and AIM appreciate the steadfast support of the Subcommittee and its continued commitment to advancing legislation important to the millions of families affected by Alzheimer's and other dementia. We look forward to working with the Subcommittee on legislative efforts to establish ARPA-H, which could make pivotal investments in breakthrough technologies that benefit people living with Alzheimer's and other dementia.

(7)

ASBMB endorses H.R. 5585 establishing the Advanced Research Projects for Health-Agency

The American Society for Biochemistry and Molecular Biology endorses [H.R. 5585 the Advanced Research Project Agency-Health Act](https://www.congress.gov/bills/117/congress/house-bill/5585?q=%7B%22search%22%3A%5B%22eshoo%22%2C%22eshoo%22%5D%7D&s=5&r=18) (<https://www.congress.gov/bills/117/congress/house-bill/5585?q=%7B%22search%22%3A%5B%22eshoo%22%2C%22eshoo%22%5D%7D&s=5&r=18>) introduced by Rep. Anna Eshoo, D-Calif., establishing the Advanced Research Projects Agency-Health agency (ARPA-H) and ensuring its autonomy and independence.

In his [remarks to the joint session of Congress](https://www.whitehouse.gov/briefing-room/speeches-remarks/2021/04/29/remarks-by-president-biden-in-address-to-a-joint-session-of-congress/) (<https://www.whitehouse.gov/briefing-room/speeches-remarks/2021/04/29/remarks-by-president-biden-in-address-to-a-joint-session-of-congress/>) in April, President Biden called for the creation of the Advanced Research Projects for Health agency “to develop breakthroughs to prevent, detect and treat diseases like Alzheimer’s, diabetes and cancer.” The creation of this agency could lead to extraordinary scientific breakthroughs, but as the ASBMB outlined in a [comment letter](https://www.asbmb.org/getmedia/404e2d89-3b58-47b3-92bb-d2b23096a662/ASBMB-Cures-and-ARPA-H-Comments.pdf) (<https://www.asbmb.org/getmedia/404e2d89-3b58-47b3-92bb-d2b23096a662/ASBMB-Cures-and-ARPA-H-Comments.pdf>) to Congressional leaders in July, the research strategy, structure and funding of ARPA-H must be clearly outlined to ensure its success.

“There is little doubt that a DARPA-like agency focused on health research can lead to breakthroughs in biomedical research that can save the lives of potentially millions of Americans,” said Benjamin Corb, public affairs director for the ASBMB. “There is, however, concern over the organization, funding and focus of such an agency. ARPA-H should be strategically developed to supplement existing research efforts, not supplant funding and research priorities.”

[\(1\)](#)

strategic plans to Congress.

Said Corb, "We applaud Rep. Eshoo for authoring this bill that will ensure that the success of ARPA-H doesn't come at the expense of baseline established research goals and priorities and we look forward to working with policymakers on this issue."



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October 20, 2021

Dear Congresswoman Eshoo:

We, the undersigned, commend you for introducing the Advanced Research Projects Agency for Health (ARPA-H) Act (H.R. 5585), a bill that would authorize an important conduit for bold new health innovations. Under your legislation, ARPA-H would be positioned to empower high risk, high reward strategies aimed at rapidly accelerating medical and public health progress. We share the commitment you, other champions in Congress from both sides of the aisle, and the Administration have made to make ARPA-H a success.

We appreciate your determination to stand up ARPA-H as soon as possible and equip it with the flexibility and authorities it needs to meet its unique mission. We offer ourselves as a resource as you continue to refine the legislative text and work towards authorizing the creation of ARPA-H this year.

Thank you for your longstanding leadership as a steward of forward-thinking, patient-centric health policy, and for the crucial role you are playing in advancing ARPA-H. We look forward to working with you, your colleagues in Congress, and the Administration to make this unique medical innovation incubator a reality.

Sincerely,

George Vradenburg
Co-Founder and Chair
UsAgainstAlzheimer's

Ellen Sigal
Founder and Chairperson
Friends of Cancer Research

Christopher Austin, MD*
Founding Director
National Center for Advancing Translational Sciences

John Dwyer
President
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*Denotes those signing in their individual capacity. Organization included for identification purposes only.

Frequently Asked Questions about Facilities and Administrative (F&A) Costs of Federally Sponsored University Research

1. What are “facilities and administrative” (F&A) costs?

F&A costs – also referred to as “indirect costs” – are essential costs of conducting research. The federal government’s longstanding recognition and payment of these costs has helped U.S. colleges and universities build and support the required research infrastructure that has made the American research enterprise the best in the world.

When the government provides a grant to a university for a research project, a portion (typically 67-75 percent) of the funds are distributed directly to the research team. This “direct costs” portion supports researcher salaries, graduate students, equipment, and supplies. Another portion (typically 25-33 percent) covers necessary research infrastructure and operating expenses that the university provides to support the research. These research expenses – officially called facilities and administrative (F&A) costs – include: state-of-the-art research laboratories; high-speed data processing; national security protections (e.g., export controls); patient safety (e.g., human subjects protections); radiation safety and hazardous waste disposal; personnel required to support essential administrative and regulatory compliance work, maintenance staff, and other activities necessary for supporting research.

2. Why does the federal government provide support for F&A costs of research?

F&A costs are research costs. Universities and the federal government have a long-standing and successful partnership that grew out of World War II. The federal government relies on universities to conduct research in the national interest. This includes research aimed at meeting specific national goals such as health and welfare, economic growth, and national defense. Performing research on behalf of federal agencies incurs a variety of costs that would not otherwise exist for universities. Universities – not the federal government – assume the risk of building the necessary infrastructure to support this research in anticipation that their research faculty will successfully compete for federal research grants and thus the university will be reimbursed for a part of the associated infrastructure costs.

3. Do universities contribute any of their own funds towards research?

Yes. Universities are the second leading sponsor of academic research and development (R&D). Federal data show that colleges and universities pay for more than 24 percent of total academic R&D funding from their own funds. This university contribution amounted to \$16.7 billion in FY15, including \$4.9 billion in unreimbursed F&A costs. These institutional commitments to academic R&D significantly exceed the combined total of all other non-federal sources of support for academic R&D: state and local government, industry, and foundation, support was at 6 percent each in FY15 and other non-federal sources provided 3 percent in FY15. Federal spending on higher education R&D has continued to decline and was just under \$37.9 billion in FY15, or 55 percent of all funding for academic R&D (See figures 1-2).¹ While universities contribute significantly to the costs of research, these institutions continue to be stretched thin. State support for public universities has declined greatly over the past 20 years and, in many cases, universities are educating more students. The notion that universities should cover even more of the costs of conducting research for the federal government is not realistic.

4. Do universities ‘profit’ from the F&A costs they receive associated with federal research grants?

No, universities absolutely do not make gains from their F&A recoveries. Universities are not even fully paid for the expenses they incur to provide the necessary infrastructure and support to conduct federal research. As stated above, in FY15 universities contributed approximately \$4.9 billion in facilities and administrative expenditures not reimbursed by the

government, many of which were not covered because of existing Office of Management and Budget (OMB) limitations on the amount the government can support universities for administrative and compliance related expenses, including federal mandates.²

5. Has the university contribution to research been increasing or decreasing?

Increasing. Over the past several years, the share of institutional support that colleges and universities provide to support research conducted by their faculty has grown faster than any other sector. This growth in institutional spending on R&D has come at the same time that federal support has been declining (see figure 3).³ The increase in institutions' support for the R&D they conduct is due in part to the rising compliance costs associated with increased federal research regulations and reporting requirements. Despite the increasing administrative costs required for compliance, the amount universities can receive from the government for these costs has been capped at a flat rate by OMB since 1991. This cap *only* applies to higher education institutions. Unlike other sectors that conduct government research, universities must therefore subsidize compliance costs from their own financial resources.

6. Has the percentage of federal funding for F&A costs changed over time?

No. F&A costs recovered by research institutions have remained flat for over 15 years. For example, the National Institutes of Health's percent of total funding going towards F&A costs has remained unchanged, at approximately 27-28 percent of total funding, for more than a decade (see figure 4).⁴

7. How much does the federal government pay for university F&A expenses compared to what it pays other government research performers such as the national laboratories and industrial contractors?

Generally, past studies suggest that total F&A costs for university research are slightly less than those costs for other research performers. A study in 2000 by the RAND Corporation found universities had the lowest percentage classified as F&A (31 percent). Federal laboratories were somewhat higher at 33 percent and industrial laboratories were higher still at 36 percent. This demonstrates that universities are efficient performers of research.⁵ Unfortunately, a comparable study to the RAND study has not been undertaken in recent years. Such a study would be welcomed by the university community.

Additionally, as indicated under the previous question, the federal payment to universities for their F&A costs does not cover the full costs to their institution. This is unlike other sectors that receive full compensation for all their costs. The federal government has smartly invested in university-based research: F&A costs at universities are lower than other sectors, the government does not pay a profit to universities like it must for industry research performers, there is a university-specific cap on the amount the government will cover for administrative expenses, and the system of agency oversight ensures universities continue to be excellent stewards of federal taxpayers' dollars.

8. Why do foundations pay less for F&A costs than the federal government does? Is the federal government subsidizing the infrastructure required to do foundation-sponsored research?

Comparing what can and cannot be charged to a federal grant versus a foundation grant is an "apples to oranges" comparison since foundations categorize and pay grant-related expenses very differently than the federal government does. For example, foundations often categorize some items as direct expenses that federal rules require to be counted as F&A expenses. This further underscores that direct and F&A costs are all part of total research costs and are inseparable when it comes to the actual conduct of research.

To the extent that a foundation does not pay for certain F&A expenses, these costs must be covered by the institution. OMB rules ([2 CFR Part 200 - Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards](#)) specifically require universities to ensure the federal government does not subsidize non-federally sponsored research activity – including research and associated infrastructure costs performed by universities for private foundations – in their support for F&A expenses.

Additionally, as previously noted, after World War II the federal government consciously chose to encourage universities to conduct research on its behalf to help achieve national goals. A core tenant of the partnership between the federal government and universities is that the government shares in the costs of research by providing universities with competitively awarded grants to support the people, tools, *and infrastructure* necessary to conduct high-quality research for the nation. Historically, most foundations view their grants as supplementing research that scientists are already conducting. To this day, most foundation research funding is viewed as supplementing existing federal and non-federal research.

Finally, foundation funding for university-based research remains a small proportion of total academic R&D funding (only 6 percent) compared to federal funding (55 percent) and the funding provided to support academic R&D by the colleges and universities themselves (24 percent).

9. Are federal F&A cost payments used to subsidize other campus accounts, such as athletics or construction?

No. OMB rules ([2 CFR Part 200 - Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards](#)) require that F&A cost reimbursements can *only* be based on federally funded research space and related research activities, not education or other university facilities or activities.

10. Is it true that universities with F&A rates over 50 percent spend more than half the grant funds they receive from the federal government to pay for F&A costs?

No. A university's F&A cost rate is *not* a percent of the total grant, but rather a percentage only of the research project's direct costs. Currently, the average amount paid to universities for F&A costs is approximately 25-33 percent of the total amount of a grant. (Campuses with medical centers tend to be closer to 33 percent because of the increased costs and expenses involved in providing for medical research facilities.)

11. How does the F&A rate determine how much a university receives for F&A costs on a grant?

Here's how it works: To determine the level of F&A expenses the federal government will cover, every 3-4 years, the agency responsible for setting a university's F&A rate (either the Department of Defense Office of Naval Research or the Department of Health and Human Services) will comprehensively audit and assess these shared costs to determine the appropriate federal share based upon specific costs that have been deemed allowable expenses by the OMB. The overall figure is ultimately calculated as a *percentage of the amount the federal government awards for direct research costs* (*not* a percentage of the overall funds, the figure most people see).

For example, after reviewing all the expected costs and considering past research projects, a university and the federal government may determine that an amount equal to 50 percent of direct research costs is appropriate for the federal government to contribute toward F&A costs. In that case, if the federal government awards a university \$300,000 for the direct research portion of a grant, then it also awards \$150,000 for F&A costs, for a total of \$450,000. These overall institutional F&A cost rates are then applied uniformly to each grant at the university to avoid the very tedious, expensive and inefficient process of computing the F&A expenses for individual awards – which would add additional costs for both the government and the university.

12. Why do F&A cost rates vary between institutions?

Federal agency officials and university administrators predetermine an overall percentage of allowed F&A costs to be paid, based on documented historical costs and cost analysis studies. The final rates allowed for F&A expenses are established based on a rigorous review and audit of the actual funds previously spent for such costs. F&A cost rates vary from institution to institution because construction, maintenance, utilities, and administration costs vary by institution and by region. Additionally, F&A rates depend upon other factors such as the age and condition of facilities and buildings and the amount of renovation and construction needed to house certain types of research projects. For example, the F&A costs for a biomedical research facility built in an urban area that experiences earthquakes is different than an engineering research facility built in a rural area.

13. How would universities cover F&A costs if the government cut back on the amount it would reimburse?

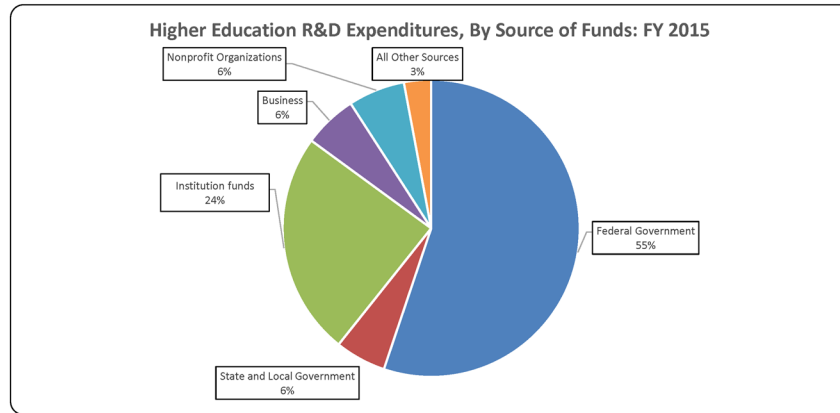
Universities have a limited number of funding sources. The primary funding sources for research universities to fulfill their educational missions of teaching, research, and service are: tuition, research grants, cooperative agreements and contracts, philanthropy, endowment income, and state appropriations.

A reduction of federal F&A payments would result in one or more of the following:

- The inability of universities to accept research awards from, and conduct research on behalf of, federal agencies;
- The deterioration of research facilities as the financial risk to build new facilities or maintain existing ones becomes too great to invest institutional funds;
- The inability to sustain required support staff and infrastructure required to comply with government regulations; this could threaten the health and safety of patients, researchers and students;
- A reduction in the pipeline of trained scientists and engineers in the workforce due to reduced research training opportunities at universities.
- An increase in tuition rates, an action which universities would not want to take.

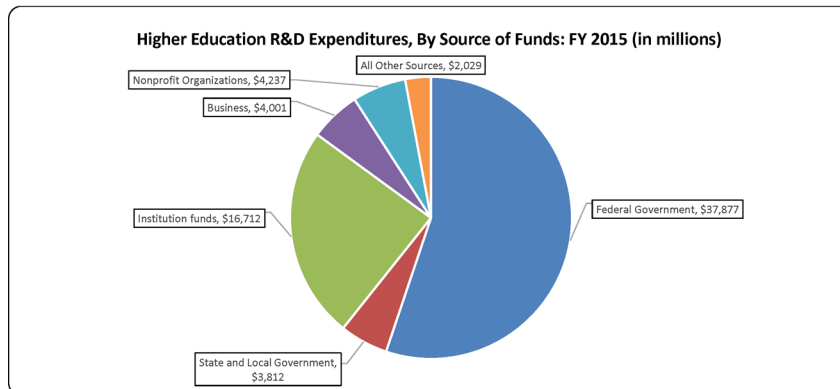
Bottom Line: *Cuts to F&A research costs are cuts to research. If such cuts are made, they will reduce the amount of research universities and their scientists can conduct on behalf of the federal government to achieve key national goals to improve the health and welfare of the American people, grow the economy, and enhance our national security.*

Figure 1



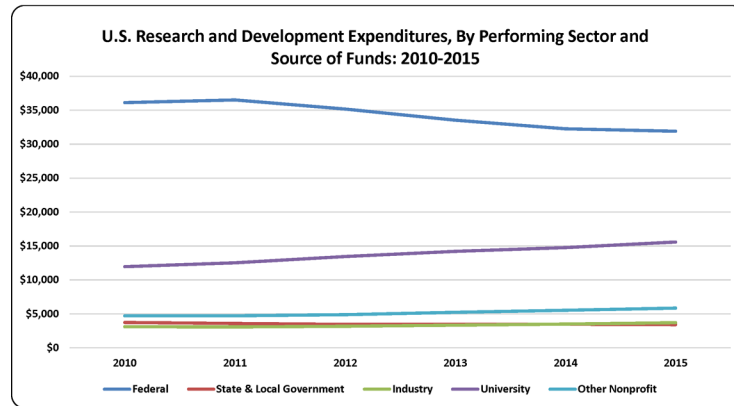
Source: NSF, National Center for Science and Engineering Statistics, Higher Education Research and Development Survey

Figure 2



Source: NSF, National Center for Science and Engineering Statistics, Higher Education Research and Development Survey

Figure 3



Source: NSF, National Center for Science and Engineering Statistics 2017, National Patterns of R&D Resources: 2014–15 Data Update

Figure 4

NIH Direct and F&A Awarded (Dollars and Percent)

Fiscal Year	Direct Awarded (000s)	F&A Awarded (000s)	Total Awarded (000s)	Direct as a Percent of Total	F&A as a Percent of Total
FY2002	12,822,068	4,835,456	17,657,524	72.6	27.4
FY2007	15,387,745	5,876,060	21,263,805	72.4	27.6
FY2012	15,978,032	6,182,900	22,160,932	72.1	27.9
FY2016	16,899,936	6,407,203	23,307,139	72.5	27.5

Source: Congressional Justification of the NIH FY2017 budget request; Overview of 2017 President's Budget

¹ National Science Foundation, National Center for Science and Engineering Statistics, Higher Education Research and Development Survey. Table 2: Higher education R&D expenditures, by source of funds: FYs 2010–2015.

² National Science Foundation, National Center for Science and Engineering Statistics, Higher Education Research and Development Survey. Higher education R&D expenditures, by highest degree granted, institutional control, and type of cost: FYs 2011–15.

³ National Science Foundation, National Center for Science and Engineering Statistics. 2017. National Patterns of R&D Resources: 2014–15 Data Update. NSF 17-311. Arlington, VA. TABLE 2. U.S. research and development expenditures, by performing sector and source of funds: 1953–2015

⁴ Congressional Justification of the NIH FY2017 budget request; Overview of 2017 President's Budget.

⁵ Goldman, Charles A., Traci Williams, David M. Adamson and Kathy Rosenblatt. Paying for University Research Facilities and Administration. Santa Monica, CA: RAND Corporation, 2000. https://www.rand.org/pubs/monograph_reports/MR1135-1.html.



February 7, 2022

Dear Chairwoman Eshoo, Ranking Member Guthrie, and Members of the Health Subcommittee,

I am writing to applaud your bipartisan efforts to create a new Advanced Research Projects Agency for Health (ARPA-H). As the leading biotech platform innovation firm, Flagship Pioneering prides itself on asking bold and provocative questions that drive our innovative science forward, often in unprecedented ways. So as we consider the ambitious remit of a proposed new ARPA-H, we would like to pose this question to the Subcommittee -- What if we could create a future largely free from disease?

Over the past two years, the world has experienced the devastating collision of the “fast” pandemic of COVID-19 with the “slow” pandemics of obesity, diabetes, cancer, neurodegeneration, and other chronic disease. The non-elderly with such underlying health issues were most likely to suffer serious illness or death from COVID-19. Our communities, particularly the underserved, have been hit so hard not only because we were unprepared for pandemic threats, but also because we suffer from insufficient health resilience. Too many people were too vulnerable because of their poor health — but it does not have to be this way.

One lesson? We have been too complacent about disease. Our healthcare and medical product innovation systems are actually *sick care* systems: they are almost entirely focused on the diagnosis and treatment of disease rather than on protecting, maintaining or improving health. By waiting for disease to manifest, outcomes are worse and costs are higher — for both society and afflicted patients.

We believe that an alternative, proactive paradigm can be built, so that people live disease-free for longer: adding years to life and life to years. By focusing on the period before sickness manifests, when people are seemingly healthy, we can preempt disease. During these periods of pre-disease (before we are patients), we know that underlying physiological changes have begun that indicate that a trajectory toward disease has commenced. By proactively identifying disease precursors and the novel biomarkers of a pre-disease state, we can find new ways to intervene earlier to reverse, prevent or postpone disease. We at Flagship call this preemptive health: the application of leading-edge biological sciences and digital technology to traditional population-level health goals. This is an urgent problem and requires innovative approaches that expedite the clinical development and regulatory pathways.

We believe ARPA-H can aid this revolutionary paradigm shift from our current sick care system to a true healthcare system by spurring development of truly transformational technologies that preempt progression of disease at much earlier stages. By marshalling its resources, access to large research and biological datasets, advanced technologies such as AI and machine learning, partnerships with industry, and risk-taking culture, ARPA-H can help us tackle our most scientifically challenging diseases in novel, use-driven ways aimed at developing targets and technological strategies for early disease intervention.

Moreover, multidisciplinary efforts could be aimed at creating the scientific foundations for a new regulatory framework that should be created — one that would provide a transparent roadmap for facilitating efficient innovation for pre-disease detection and intervention, something the current FDA regulatory paradigm is not designed to do. This is the type of breakthrough R&D which it is challenging

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for any single company to effectively pursue, but which would be essential to fulfill ARPA-H's overall mission to dramatically accelerate the development of game-changing technologies and medicines for patients.

We do not believe this approach would duplicate or intrude upon the broader basic research function of the National Institutes of Health. Rather, we believe ARPA-H can and should focus on leveraging this massive federal investment in basic research to identify and support mechanisms for transformational change aligned with its ambitious mission.

As the Subcommittee develops authorizing language for ARPA-H, we would encourage you to consider ways to incorporate this critical concept of preemptive health into the mission of this new agency, and Flagship stands ready to assist you in any way.

Sincerely,

A handwritten signature in blue ink, appearing to read "N. Afeyan", with a horizontal line extending from the end of the signature.

Noubar Afeyan, PhD.
Founder & Chief Executive Officer
Flagship Pioneering

February 1, 2022

The Honorable Anna G. Eshoo
Chairwoman
Subcommittee on Health
House Energy and Commerce Committee
272 Cannon House Office Building
Washington, DC 20515

The Honorable Brett Guthrie
Ranking Member
Subcommittee on Health
House Energy and Commerce Committee
2434 Rayburn House Office Building
Washington, DC 20515

Dear Chairwoman Eshoo and Ranking Member Guthrie,

ARPA-H has the potential to be an extremely impactful undertaking for our Nation and getting it right is no small matter. The creation and sustainment of any organization tasked with fostering innovation and leaps forward requires a very deliberate approach, as it is extremely easy to get the equation wrong.

Innovation in this day-and-age is very much about making advantage of the ever-increasing speed of technology cycles combined with leveraging the significant investment from the commercial sector combined with seeding/harvesting research/academics at scale. Translation of innovation by/with/into government requires the utmost consideration and deliberate approach in achieving a desired outcome, as institutional government is not currently designed to be the optimum environment. Success is as much about what should not be done as what should be done. What should be done is to build a standalone construct directly funded and insulated from large bureaucratic institutions and politics and recruit proven successful leadership from a highly competitive part of the economy with autonomy to create an agile and fast culture by recruiting the best-and-brightest constructive minds who can ultimately produce the intended results. What should not be done is to subjugate ARPA-H to a large and slow-moving bureaucratic government structure, like the NIH, or to the leadership of any career bureaucrats. If NIH is the home of ARPA-H, you would be better off not wasting the money, time, and opportunity. Likewise, you will want to select your leadership from the ranks of the fastest evolving part of the nation and economy. Innovation inherently includes some failure, and, failing-fast and recovering-quickly is important and characteristically intrinsic to successful leaders operating at competitive speed. Please do it right.

I am including some of my background/experiences below, to create some context for my advice above.

As an Entrepreneur I have been building the most advanced healthcare and medical device ventures over 30 years in the Silicon Valley. I founded and led the first eCommerce system for

medical supplies streamlining the healthcare supply chain and saving lives; I founded and led the earliest Software as a Service (SaaS) company for designing and equipping high tech hospitals better and faster thereby saving lives; and I led the first breakthrough Artificial Intelligence software company in medicine saving the lives of stroke patients. I have created both private and public companies, and all these ventures have stood the test of time and continue to be leaders. I understand innovation in healthcare and medicine and translating such into constructive production.

As an Academic with multiple advanced degrees in engineering and biomedical physics from our Nation's premier institutions and programs, I translate innovation from academics into commercial ventures. As an Adjunct Professor at the Stanford University School of Medicine, my primary responsibility is working with clinical and academic faculty to bridge academic innovation into commercial solution and venture creation. I have been successful and have also been witness to failures. I understand academic research innovation and translating such into commercial successes.

As a Citizen I answered the call of the Nation and am currently assisting the Department of Defense as a Director of the well-known Defense Innovation Unit. I work with the Leaders of the Department and the Commanders of the Military, and across the chain-of-command to the warfighters. I have advanced innovative cyber and telecommunications capabilities into the DoD to strengthen the Nation's security, and I work closely with the teams responsible for doing the same with artificial intelligence, autonomy, energy, human systems, and space. The White House and other Cabinet Departments are engaged with my work and approach. I have been successful and have also been witness to failures. I understand commercial innovation and translating such into government.

Please feel welcome to contact me directly if you need further detail or color.

Respectfully Submitted for the Congressional Record,

Dr. Jeffrey H. Kleck



DATE: February 7, 2022

TO: The Honorable Anna Eshoo, Chairwoman
The Honorable Brett Guthrie, Ranking Member
U.S. House Energy and Commerce Committee Subcommittee on Health

FROM: David Arons, Chief Executive Officer
Danielle Leach, Chief of Community and Government Relations
The National Brain Tumor Society

National Brain Tumor Society submits the following statement for the February 8, 2022, U.S. House Energy and Commerce Committee Subcommittee on Health hearing, "*ARPA-H: The Next Frontier of Biomedical Research*." We respectfully request that this statement be entered into the hearing record.

National Brain Tumor Society (NBTS) is the largest patient advocacy organization in the United States committed to curing brain tumors and improving the lives of brain tumor patients and their families. Our vision of conquering and curing brain tumors is powered by our partnerships across science, health care, policy, and the business, nonprofit, and governmental sectors. We fund treatment-focused research and convene those most critical to curing brain tumors once and for all.

We support the Committee's work to bring attention to the proposed ARPA-H program and are pleased that cancer will be one of the primary focuses of the program. The Committee's important work will be further supported by President Biden's recently reignited Cancer Moonshot initiative. NBTS is supportive of both ARPA-H and the Cancer Moonshot initiative and hopes the concerted effort and collaboration across all government agencies and research programs can create the cures and quality of life our brain tumor community urgently needs.

Today, an estimated 700,000 people in the United States live with a primary brain tumor. More than 88,000 new diagnoses are expected in 2022, and an estimated 150,000 additional cases of metastatic brain cancer are further anticipated. A diagnosis comes with a severe impact to patients and loved ones, and certain brain tumors are among the most life-threatening forms of cancer. Brain tumor patients and loved ones need breakthroughs now.

Brain tumors are an excellent focal point for ARPA-H as solving the challenges associated with their treatment offers the potential to yield significant progress for many other disease areas, even beyond cancer. For example, ARPA-H could spearhead innovation in technologies to open the blood-brain barrier to promising drugs that

could benefit patients with brain tumors and other neuro-degenerative diseases. It could also bring forward novel liquid biopsy approaches to evaluating the existence and growth of brain tumor cells and may someday bring about early detection for brain tumors that does not exist today. Finally, the new program, through pushing forward the field of radiographic imaging, could potentially open up new opportunities to know if investigational treatments are working against brain tumors and other brain related diseases in less and non-invasive ways. We urge that as ARPA-H is authorized it be instructed to be inclusive of patient experience and patient advocacy so that the new program is true and authentic to those it is ultimately serving.

ARPA-H is a bold and timely opportunity to build on and leverage partnerships between the National Institutes of Health (NIH) including the National Cancer Institute and industry to launch a portfolio of transformational projects to help brain cancer patients and many others. We offer to serve as a resource for the Committee as it addresses ARPA-H and share our thoughts. We look forward to working together, and if you have any questions or would like additional information, please contact Danielle Leach, Chief of Community and Government Relations, at dleach@braintumor.org.

**STATEMENT FOR THE RECORD**

Submitted by
Rajarshi Banerjee, M.D., Ph.D., MSc., MRCP
Chief Executive Officer, Perspectum

“ARPA-H: The Next Frontier of Biomedical Research”
Hearing before the Subcommittee on Health
Committee on Energy and Commerce
February 8, 2022

Chair Eshoo, Ranking Member Guthrie, Chairman Pallone and Ranking Member
McMorris-Rodgers:

Thank you for the opportunity to submit testimony today on the need and opportunities arising from the United States’ commitment to modernizing biomedical research infrastructure to keep pace with the astounding and rapid developments which are occurring almost daily in science. As a scientist, medical doctor, and co-founder of a diagnostics company, Perspectum, I commend you for your foresight in scheduling this examination of one of the largest issues facing medicine and our health care delivery system today.

In particular, I appreciate the opportunity to continue our dialog on how research can improve the diagnosis, treatment and potentially even curative treatments for long-COVID-19, or as some call it, “long-COVID,” or Post-Acute Sequelae of SARS-CoV-2 infection (“PASC”).

At the outset, I hasten to recognise Oversight Subcommittee Chair Diana DeGette and former Chair Fred Upton for their vision, foresight and determination in drafting and advancing the ARPA-H legislation. That there are at last count 80 cosponsors of H.R. 6000 speaks volumes about it, not only the need for this bill, but also the overwhelming support it is receiving in Congress.

Indeed, it is important to recognise the landmark achievement of the predecessor law, and at Perspectum we hail the Committee’s persistence and leadership in drafting, pushing to enactment, and then monitoring implementation of the landmark 21st Century Cures law (P.L. 114-255), which has done so much to spur innovation in health care research, treatment, and delivery. Your deep commitment to improving the lives of patients is evident by this substantial work, and it is even more impressive that you are now advancing the follow-on, comprehensive, CURES 2.0 bill.

Today, I would like to provide the Subcommittee with the benefit of Perspectum’s views on long-COVID, a family of diseases to which we have devoted considerable energy from the start of the pandemic. We are keenly aware, and are especially heartened, that the authors recognise the importance of advancing knowledge of long-COVID by addressing it in the first

section of the bill. It is my hope this legislation can be enacted this year and I offer my continued assistance to members and staff whenever needed.

Who We Are:

A brief mention about my background may help you put my remarks in context. I studied medicine at Oxford, and became interested in acquired heart and liver disease, which were alarmingly on the rise driven by obesity and alcohol use, conditions which are unfortunately all too present in the United States as well. I realized that I wanted to play a role in improving care for these patients and focused on developing customized solutions to deliver better outcomes to promote what we call in Britain, “kinder healthcare.” This led me to build a medical technology company, assemble a highly capable multidisciplinary team with many great diagnostic scientists, engineers and clinicians, and direct our focus to work on these challenges, starting first with liver disease.

Perspectum now is a leading commercial-stage, precision health company based in the United Kingdom with offices in the United States. Our approach to patient care draws on the expertise of the renowned physicians and scientists who lead our company, and we collaborate with world-leading experts on metabolic diseases, cancer, diabetes and other chronic diseases to push forward research. In offering advanced diagnostic solutions to doctors, we can support better decision-making, personalized care for patients, and better outcomes.

At Perspectum, we are very proud of our flagship product, LiverMultiScan, which has been cleared by the Food and Drug Administration for the non-invasive assessment and monitoring of liver disorders that may include nonalcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH), a severe form of fatty liver disease. LiverMultiScan is now being used in over 250 sites in the US, and is part of the Medicare and AIM pathways for the safer evaluation of liver disease, replacing liver biopsy. We have other FDA-approved products, including those to support precision surgical decision-making for hepatologists and provide clinicians with highly-specific tools to monitor biliary diseases, such as primary sclerosing cholangitis (PSC).

As a company, Perspectum is committed to innovation and matters of public health and healthcare.

Our Response to the Emerging Covid-19 Pandemic:

The long-term impacts of COVID outside the lungs were not known in the period of March-April, 2020 when COVID first was discovered and then declared a pandemic. Perspectum already had many great medical innovation and clinical scientists, so it was only natural to focus our energies on COVID-19.

We undertook the world’s largest study of mapping organ health in ‘post-COVID’ individuals. We enabled existing mobile MRI scanners on site at our main office with our

advanced software services to look at multiple organs in the torso, using a single 30-minute scan to find out if a patient has sustained organ damage by a disease. We became the first to show that organ damage can occur in COVID patients even if they have not been hospitalized. Our preliminary figures indicated that, four to five months after infection, almost 70 percent of COVID patients with persistent symptoms had sustained damage to one organ, and a quarter of these have two or more organs damaged (Dennis et al. 2021, referenced below).

Compelled by findings of our recently published community-based clinical study (designed and conducted by a Perspectum team in Oxford and our collaborators entitled, “Multiorgan impairment in low-risk individuals with post-COVID-19 syndrome: a prospective, community-based study,” [Dennis et al. \(2021\). BMJ Open, 11\(3\), e048391¹](https://doi.org/10.1136/bmjopen-2021-027391)), we are continuing to explore the possibility that there are unique health issues facing women presenting with Long-COVID. Of the individuals in our community study, 71% were females and 19% had been hospitalized with COVID-19. Impairment in the liver, heart or lungs was associated with further organ impairment in 63%, 62% and 48% of individuals, respectively. I also currently serve as a team member of the largest clinical long-COVID study to-date called [STIMULATE-ICP2](https://www.stimulate-icp.org/) (Symptoms, Trajectory, Inequalities and Management: Understanding Long-COVID to Address and Transform Existing Integrated Care Pathways), led by University College London Hospitals NHS Trust and University College London. The 2-year study is designed to deliver the needed knowledge to scientists and clinicians to improve patient care and to inform policymakers, while collecting real-world data at scale.

Real-Time Revelations:

The long-COVID communities of researchers, clinicians and patients are extremely gratified that Congress had the wisdom to provide \$1.15 billion in funding to the National Institutes of Health for grants which will begin to answer the myriad mysteries of PASC, including whom it affects, for how long, and how they should best be treated.

From our work, we become more and more convinced about the need to devote additional resources to long-COVID – to help patients, to identify how best to treat the range of illnesses long-COVID embraces, and to determine the extent and duration of post-COVID illness, among many issues. Even now in our third-year of the pandemic and despite the best efforts of researchers and clinical medical experts, we still have not identified sound clinical treatment pathways for long-COVID patients, do not understand whom it affects and for how long, and are still addressing the PASC crisis in “real-time,” while many people are also now dealing with the after effects of COVID-19 infections persisting.

¹ <https://bmjopen.bmj.com/content/11/3/e048391>

² <https://www.stimulate-icp.org/>

As you may recall, as CEO, I submitted testimony to the April 28, 2021, Health and the Environment Subcommittee hearing on Long-COVID in which Perspectum observed five key points that must be considered in any on-going study of long-COVID:

- 1) In the majority of persons whose COVID does not resolve in three months, there can be significant organ damage which should be recognised early;
- 2) Long-COVID is a multi-system illness that must be treated holistically;
- 3) We have no idea how long it will persist in a patient, and this could engender a whole new cohort of the disabled, especially among healthcare workers;
- 4) We are beginning to see signs that the health care delivery system cannot keep up with the need for patient treatment; and
- 5) More information needs to be developed about the disproportionate impact of long-Covid on certain patient populations, be it race, income, age, geography or pre-existing conditions, to name a few.

These observations largely remain true today and this supports the focus of H.R. 6000.

Comments on Sec. 101, "Further Understanding the Implications of long-COVID":

We are enormously appreciative of the prominent and early long-COVID language you included in the CURES 2.0 bill; it is to be noted that you obviously understand the importance of work to help patients in this area because you included as the very first section, Sec. 101, language on the "Further Understanding the Implications of Long-COVID." It is that language on which we wish to make several recommendations as follows.

First, at the outset, we urge that efforts be undertaken to develop a common understanding of the definition of "long-COVID" – whether in your legislation or by some other administrative, congressional or other action. It is extremely hard to measure the extent of PASC or know how long to monitor its progression in patients as well as our success in addressing it, without a common understanding of what and how "long" long is. Understanding these things is of the utmost importance from the perspective of patients' physical and mental health. We note that the World Health Organization (WHO) recently published a clinical case definition of post-COVID. Although the WHO definition has been criticized by some as lacking, we concur with the motivation behind the WHO's action – that a lack of consensus on the time of onset and length of symptoms could impede our complete understanding of the extent and duration of PASC; this undoubtedly affects medical research and the utility of study results.

Other recommendations on the specific subsections of Sec. 101: “Further Understanding the Implications of Long-COVID”:

General Comment: As a general comment on the purpose of Sec. 101, we believe that this is an important and certainly a necessary goal. We also appreciate that the implications of PASC are far from being identified totally. That said, we urge that you move beyond “study” to action on long-COVID where possible and especially in clinical settings and care, as there are published data showing that patients with long-COVID are at higher risk of death, disability and rehospitalisation.

Perspectum respectfully suggests you have the opportunity to play a leadership role in strengthening the US government’s response to long-COVID by broadening this language. For example, this could be accomplished by a sectional title change:

We suggest that the title embrace the notion of encouraging action on the range of issues associated with long-COVID, beyond the national coverage study. We recommend the Section 101 title read “Establishing a Framework for Priority Action on Long-COVID.”

While there is substantial funding being devoted to long-COVID research, and more to come as funding for programs under the ARPA-H entity you authorize gets underway, even so there is need for us to act now where we can. The job is substantial, spanning all the public health agencies as well as the Social Security Administration and perhaps the Department of Labor (e.g., the Office of Disability Employment Policy and the Occupational Safety and Health Administration) and the Internal Revenue Service among others.

Authority for New Coordinating and Monitoring Bodies: For this reason, we respectfully request you consider establishing two coordinating and monitoring bodies. The first would be an inter-agency Task Force which will bring together all of the Federal government’s myriad agencies who address long-COVID. The second would be a new “Office of Long-COVID” established under the authority of the Assistant Secretary for Health (ASH) at the Department of Health and Human Services (HHS).

Virtually every public health agency is involved in PASC in some way, from the Centers for Disease Control and Prevention to the National Institutes of Health, but also agencies such as the Health Resources and Services Administration which we believe will play a growing role as the need for increased service delivery in this population becomes more evident.

Over the years, the ASH has played a leadership role in coordinating the government’s response to health crises, for example with AIDS in the mid-1980s. So, this would be a natural home for such an effort. That said, if you determine a broader need exists so that programs in human services could also be embraced, a new office could be established at secretarial level.

While we understand the natural reluctance to create bureaucratic entities, in this case there is an urgent need for such a coordinating body, which can both provoke action and

monitor the range of results. Likewise, such a need exists across government agencies. If there are concerns about the length of operations of these offices, they could be term-limited with the possibility for reauthorisation in the future.

Sec. 101(a)

Regardless of who is the lead in Federal governmental long-COVID efforts, we think there is a need for further understanding the implications of a number of issues associated with long-COVID beyond what is in your draft legislation.

Sec. 101(a)(1)

Additional requirements for the study: For the Survey, you may want to direct the Department of Health and Human Services to study current funding and sources for coverage of long-COVID in both the public and private sectors; this would complement the current language which surveys patients only. Further, we suggest you consider providing guidance on how “large” the national survey is – to make certain it adequately reflects a range of geographic areas, including rural and urban, a range of age groups, young to old, and a range of persons from varying socio-economic backgrounds, races, and genders. Health inequalities have been highlighted by COVID-19 and apply to long-COVID patients as well.

Additional topics for the study: We also recommend that your draft go beyond assessing the broad topics of health care coverage, long-term care coverage, and disability coverage to address problems more specifically with factors such as:

-Eligibility for coverage in these three areas:

- *for primary care visits*
- *access to diagnostics,*
- *follow-up with specialists, and*
- *on-going care and rehabilitation needs, including support to return to employment.*

-Eligibility for services based on issues such as lack of an initial positive COVID test (discussed much at the April 28 hearing); and,

-The need for a standardized definition of disability to ensure quick access to disability coverage.

Sec. 101(a)(2)

Survey Report: We agree it is important for Congress to have an expedited report about the coverage survey; that said, it might be helpful to require that in writing, in the report, that the Secretary or his designee provide a description of who was surveyed when and where, and a discussion of the answers to the above questions we suggested you pose.

Sec. 101(b)(1)

Learning Collaborative: Page 4, lines 1-2, you may want to make clear that the representatives should be from key sectors of the health care community “who have expertise in long-COVID.”

Sec. 101 (c)

COVID Scientific Research for Children: We heartily endorse the addition to your proposal of this authorization for NIH grants to research the long-term effects and treatments of COVID-19 in children. We are starting to engage in such research in the UK and welcome any future collaboration.

Sec. 101 (d)

Study on Disparities in Long-COVID: Additionally, we welcome this addition to the previous draft, which will authorize a National Academy of Medicine study on disparities in racial and ethnic minority groups on the diagnosis of, severity of symptoms, access to care, and treatment for long-COVID. As the pandemic progresses, we are finding such disparities more and more, and their identification can only improve diagnosis and treatment outcomes.

Sec. 101 (e)

Education and Dissemination of Information with Respect to Long-term Symptoms of COVID-19: As previously cited, we are concerned about the relative lack of attention given to managing long-COVID clinically, and therefore a public education program at HHS is very welcome. Likewise, dissemination of information to providers under this program is a welcome addition to the bill, although we caution any such program must not only be flexible enough to provide information in as close to “real-time” as possible. The information dissemination must also embrace the full range of issues associated with PASC, including appropriate diagnostic tools and treatment options.

Funding for Programs Authorized in Sec.101: We are heartened that H.R. 6000 has now allocated specific authorizations for programs contained in this section, in contrast to the “such sums” authorization in the previous draft. This is an improvement. Additionally, we note the relative lack of public discussion and thus priority devoted to long-COVID compared with COVID itself. As we watch the real possibility that this pandemic will become endemic, there is not enough focus on the fact that long-COVID most certainly could linger.

By-Pass Budget: As you know, the National Cancer Act of 1970 provided a special authority that allows the National Cancer Institute to submit a “bypass” budget directly to The White House without Department review. The intent was to make certain that cancer research received what the scientific community felt was necessary, unimpeded by more political considerations. Given the importance of continuing PASC research, we suggest you might

consider authorizing the HHS to submit a “bypass budget” for some or all of the long-COVID programs authorized in H.R. 6000. If there are concerns about this precedent, it could be time-limited.

Potential Addition to Sec. 101:

NIH Report: Given that the majority of long-COVID activities are currently taking place at the National Institutes of Health, and recognizing the large appropriation for those activities you provided to NIH, you may want to consider requesting a brief-but-comprehensive biannual report (or some other patient-friendly medium) from the agency on its COVID research activities. While we would not want to divert NIH’s work, it is important that the patients know what research is being undertaken and where should patients and their families wish to participate or learn more. Clinicaltrials.gov may be too specific and not easily navigable for these purposes.

Conclusion:

In closing, Madame Chair and members of the Subcommittee, we at Perspectum commend your foresight in addressing the public health problem that is long-COVID. From our work over the past two years, it is clear that there is much to be learned about PASC, but we must ensure doctors and other health care providers recognise and diagnose long-COVID early in a patient’s illness. We also must develop clear clinical guidelines while simultaneously developing effective treatment pathways. I am outlining just a few of the many challenges our health care delivery systems face – and I fear we are losing precious time for many patients and their loved ones already. It is my hope that the benefit of our experience will help direct you as you move forward, and I remain available to provide the benefit of our expertise to you at any time.

Thank you for this hearing, and thank you for the opportunity to submit this testimony today.

Nellie Wild | VP Corporate Affairs
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Phenome HEALTH

November 11, 2021

The Honorable Anna G. Eshoo
Chairwoman
Subcommittee on Health
House Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

Dear Chairwoman Eshoo:

We are writing to express our strong support for the legislation you have introduced, H.R. 5585, to create the Advanced Research Projects Agency for Health (ARPA-H). It will catalyze innovation, transform big ideas, advance scientific discovery, and optimize human health.

We have spent our careers on research and clinical investigations into how to provide and deliver better healthcare to humans. Transformational advances in human understanding over the past half century, including pioneering new technologies for analyzing human biomolecules such as the explosive advances of DNA sequencing, the human genome project, a systems biology approach applied to medicine (precision medicine), and the data-driven analyses of precision population health medicine where definitive physiological, molecular, imaging, and clinical information provide fundamental new insights into human health, both for body and brain. These place us in a unique position to bring all of these technologies, strategies and computational platforms together in an integrative manner to transform health. We can now advocate a science of individual human wellness and disease prevention.

ARPA-H appears uniquely positioned to catalyze a fundamental change in medicine that is predictive, preventive, personalized, and participatory. We are on the cusp of a shift in the evolution of health care and medicine unlike anything we have seen previously. We believe ARPA-H will revolutionize the manner which government helps to usher in the era of individualized care based on a fuller understanding of the human genome and phenome and the application of these insights to individual humans.

We are particularly pleased to understand that ARPA-H will function as a distinct organization with independent management following the innovative DARPA approach at the DOE (a director and program managers who will choose the projects). We endorse the concepts that the new program managers will be serving independently and without typical peer review timelines, that up front risk taking will be considered important for projects considered by ARPA-H, and that the importance of the consolidation of relevant knowledge and diversity, equity and inclusion are high priorities. We can reach more milestones in health care when we move data from silos and employ the science of wellness integratively and longitudinally across individual lives. As designed, ARPA-H can transform how we approach individualized wellness, disease prevention and treatment over the entire spectrum of acute and chronic diseases.

Phenome Health 401 Terry Ave North Seattle, WA 98109-5234 | phenomehealth.org

We look forward to further action on H.R. 5585 that will authorize ARPA-H. We will be fully supportive of funding and have signaled our support to other Members of Congress. It is our sincere hope to be a part of ARPA-H as we make our way through another paradigm shift in science and health. We stand ready to assist you and your staff in any way possible.

Sincerely,



Lee Hood, MD, PhD
Co-Founder and Chief Strategy Officer
ISB, Seattle
CEO, Phenome Health



Michelle A. Williams, ScD
Dean of the Faculty
Harvard T.H. Chan School of Public Health



George Church, PhD
Robert Winthrop Professor of Genetics
Harvard Medical School



Ralph Snyderman, MD
Chancellor Emeritus, Duke University
Director, Duke Center for Personalized Health Care



Ed Lazowska
Professor and Bill & Melinda Gates Chair Emeritus
Paul G. Allen School of Computer Science & Engineering
University of Washington

cc: Representative Jim Clyburn, Majority Whip
Representative Cathy McMorris Rodgers, Ranking Member
Representative Kim Schrier, MD



Statement for the Record

U.S. House Subcommittee on Health of the Committee on Energy and Commerce

February 8, 2022

Submitted by: Catharine E. Krebs, PhD, Medical Research Specialist

On behalf of the Physicians Committee for Responsible Medicine, thank you for the opportunity to submit this statement for the record regarding the establishment of the Advanced Research Projects Agency for Health (ARPA-H). We request this statement be included in the record for the Subcommittee on Health's February 8, 2022 hearing entitled "ARPA-H: The Next Frontier of Biomedical Research."

The Physicians Committee is a 501(c)(3) nonprofit organization supported by over 175,000 members nationwide working for effective, efficient, and ethical medical research and product testing. We collaborate with federal and state agencies, the private sector, and academia to improve public health and medical practice.

As Congress provides the necessary framework for ARPA-H, the Physician Committee recommends the following objectives to ensure the new agency's ability to truly transform medical breakthroughs: (1) establish a strategic focus on human-specific approaches, (2) establish ARPA-H independently of the National Institutes of Health (NIH), and (3) commit to public transparency and accountability.

1. Strategic focus and investment in human-specific approaches

To achieve its goals of accelerating innovations and transforming health technologies and cures, ARPA-H must include a strategic focus on human-specific, nonanimal research. Human-specific research approaches, including tissue chips, organoids, and in silico models, use human cells, tissues, and data to better predict outcomes for patients. Not only do these approaches recapitulate human physiology, disease states, and clinical responses to drugs more closely than animals, they also permit key advantages over comparable animal-based systems, such as microenvironmental control, longitudinal monitoring, high throughput experimentation, and patient-specific modelling, all within a shorter time frame and with lower resource and ethical burdens.¹ Additionally, these innovative methods can account for complex and diverse human risk factors, helping to advance personalized medicine and reduce health disparities, a pillar of the ARPA-H concept.² Prioritizing funding for studies involving human subjects and investigating community and population health and health disparities will help address not only disparities in health outcomes, but also disparities in investigator award rates.³

¹ Ingber, Donald E. "Is It Time for Reviewer 3 to Request Human Organ Chip Experiments Instead of Animal Validation Studies?" *Advanced Science* 7, no. 22 (2020): 2002030. <https://doi.org/10.1002/advs.202002030>.

² The White House. "ARPA-H Concept Paper." Published online 2021. <https://www.whitehouse.gov/wp-content/uploads/2021/06/ARPA-H-Concept-Paper.pdf>.

³ Hoppe TA, Litovitz A, Willis KA, et al. Topic choice contributes to the lower rate of NIH awards to African-American/black scientists. *Sci Adv.* 2019;5(10):eaaw7238. [doi:10.1126/sciadv.aaw7238](https://doi.org/10.1126/sciadv.aaw7238).

In addition to improving success in translating medical discoveries to interventions for patients, a strategic-focus on human-specific research at ARPA-H would aid animal research reduction and replacement efforts, lead to a higher return on investment of federal research dollars, and help the U.S. maintain global leadership in medical research. Medical research currently relies heavily on the biology of other animal species,⁴ with as many as 100 million dogs, cats, monkeys, mice, rats, and other animals being used in U.S. laboratories each year.⁵ However, analyses of many disease areas, including Alzheimer's disease,⁶ cancer,⁷ and sepsis,⁸ demonstrate that information derived from animal experiments does not translate well to humans due to species differences in anatomy, physiology, lifespan, and disease characteristics. This lack of translation is costly⁹; around 95% of drugs fail in clinical trials after passing extensive animal testing.¹⁰ Increasingly, scientists and various stakeholder groups including the NIH¹¹ acknowledge the shortcomings of animal experiments, concluding that there is a need to develop and promote methods that are more relevant for humans.¹²

The high-risk, high-reward nature of ARPA-H provides a crucial opportunity to shift U.S. medical research away from animals and ensure global leadership in human-specific research innovation and technology.¹³ We therefore recommend that there be an explicit goal in authorizing legislation for ARPA-H to reduce research reliance on animals by including consideration of translatability to humans and reduction of animal use as explicit criteria for determining ARPA-H investments.

Experts and scholars in animal ethics and nonanimal methods can provide the ARPA-H director with global context and detailed input to advance progress in reducing medical research reliance on animals. Congress should ensure that partnerships with nonprofit organizations, including patient advocacy groups and animal protection groups, are pursued in the setting of strategic direction at ARPA-H.

⁴ Veening-Griffioen DH, Ferreira GS, Boon WPC, et al. Tradition, not science, is the basis of animal model selection in translational and applied research. *ALTEX*. 2021;38(1):49-62. doi:10.14573/altex.2003301.

⁵ Carbone L. Estimating mouse and rat use in American laboratories by extrapolation from Animal Welfare Act-regulated species. *Sci Rep*. 2021;11(1):493. doi:10.1038/s41598-020-79961-0; USDA APHIS | Research Facility Annual Summary & Archive Reports. Accessed April 24, 2021. https://www.aphis.usda.gov/aphis/ourfocus/animalwelfare/sa_obtain_research_facility_annual_report/ct_research_facility_annual_summary_reports.

⁶ Pippin JJ, Cavanaugh SE, Pistollato F. Animal Research for Alzheimer Disease: Failures of Science and Ethics. In: Herrmann K, Jayne K, eds. *Animal Experimentation*. Vol 22. Working Towards a Paradigm Change. Brill; 2019:480-516. Accessed February 4, 2022. <https://www.jstor.org/stable/10.1163/j.ctv9h2q0f.27>.

⁷ Mak IW, Evaniew N, Ghert M. Lost in translation: animal models and clinical trials in cancer treatment. *Am J Transl Res*. 2014;6(2):114-118. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3902221/>.

⁸ Seok J, Warren HS, Cuenca AG, et al. Genomic responses in mouse models poorly mimic human inflammatory diseases. *Proc Natl Acad Sci*. 2013;110(9):3507-3512. doi:10.1073/pnas.1222878110.

⁹ Animal testing and its alternatives – the most important omics is economics. *ALTEX - Altern Anim Exp*. 2018;35(3):275-305. doi:10.14573/altex.1807041.

¹⁰ National Center for Advancing Translational Sciences. "About New Therapeutic Uses." Published March 18, 2015. <https://ncats.nih.gov/ntu/about>; Thomas DW. Clinical Development Success Rates 2006-2015. Published online 2016. <https://www.bio.org/sites/default/files/legacy/bioorg/docs/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO%20Biomedtracker.%20Amplion%202016.pdf>.

¹¹ National Center for Advancing Translational Sciences. "About Tissue Chip." Published March 16, 2015. Accessed February 4, 2022. <https://ncats.nih.gov/tissuechip/about>.

¹² U.S. Government Accountability Office. *Animal Use in Research: Federal Agencies Should Assess and Report on Their Efforts to Develop and Promote Alternatives*. 2019;(GAO-19-629). Accessed August 20, 2020. <https://www.gao.gov/products/GAO-19-629>.

¹³ "On a 30-Year Mission to Replace Animal Tests with Alternative Methods." EU Science Hub - European Commission. Accessed February 4, 2022. <https://ec.europa.eu/jrc/en/news/30-year-mission-replace-animal-tests-alternative-methods>.

Authorizing language for ARPA-H should also establish that Program Managers, as selectors of projects to be supported by ARPA-H, take into consideration the following criteria, which are absent in currently proposed ARPA-H authorizing language: (a) the relevance of the project to human biology and disease, (b) the project's minimization or elimination of animals, (c) the project's inclusion of women and minorities as subjects, and (d) the diversity of perspectives and research modality expertise on the research team. Together, these criteria will help to advance translation, reduce reliance on animals, promote innovation, and foster workforce diversity.

2. Independence from the NIH

For ARPA-H to be truly transformational, it is crucial that it remains independent from the structure and culture of the NIH by being housed separately within the Department of Health and Human Services (HHS). Scientist attitudes toward animal experiments and the human-specific approaches capable of replacing them are key cultural components driving research trends and model choice.¹⁴ NIH culture, through strategic planning documents and processes, grant review procedures, and ethics policies, upholds the idea that animal experiments are a gold standard; this view would hinder the ability of ARPA-H to accelerate innovations and transform health technologies.

A recent NIH Advisory Committee to the Director working group on Enhancing Rigor, Transparency, and Translatability in Animal Research stated that “tackling the cultural incentives to keeping the status quo” will be required to improve the translatability of model systems.¹⁵ While we agree with this sentiment, the working group and the NIH both fail to understand that the biggest problem with the status quo is not that animal research lacks certain characteristics like rigor, reproducibility, and validity; it is the continued NIH reliance on animal use and its unwillingness to move away from this paradigm that stalls progress. ARPA-H must shift away from a culture of continually prioritizing animal-based methods and toward a culture that supports the development of more ethical and more translatable nonanimal methods through innovation and risk-taking. To ensure this independent culture, ARPA-H should be housed independently of the NIH.

Furthermore, housing ARPA-H at HHS would allow more seamless coordination between and collaboration with agencies other than the NIH that also play a crucial role in the prevention and treatment of disease, such as the Centers for Disease Control and the Food and Drug Administration. Transforming medical breakthroughs at ARPA-H will require a diversity of perspectives, tools, and collaborations, as well as a flexibility that are best fostered at an independent agency built from the ground up, rather than through existing structures.

3. Transparency and accountability

The U.S. commitment to the 3Rs principles of refinement, reduction, and replacement of animals in research is laid out in the Guide for the Care and Use of Laboratory Animals, the use of which is required by the Public Health Service Policy.¹⁶ Integral to this commitment are the accurate counting of animals used in experiments and the accurate reporting of federal funding dedicated to projects involving animals. It has been NIH's policy since 1985 to collect an “average daily inventory” of vertebrate animals housed in research facilities that wish to receive agency

¹⁴ Veening-Griffioen, Désirée H., Guilherme S. Ferreira, Wouter P. C. Boon, Christine C. Gispen-de Wied, Huub Schellekens, Ellen H. M. Moors, and Peter J. K. Van Meer. “Tradition, Not Science, Is the Basis of Animal Model Selection in Translational and Applied Research.” *ALTEX* 38, no. 1 (2021): 49–62. <https://doi.org/10.14573/altex.2003301>.

¹⁵ ACD Working Group on Enhancing Rigor, Transparency, and Translatability in Animal Research. NIH Advisory Committee to the Director. Accessed December 6, 2021. <https://www.acd.od.nih.gov/working-groups/cprar.html>.

¹⁶ U.S. Government Accountability Office. “Animal Use in Research: Federal Agencies Should Assess and Report on Their Efforts to Develop and Promote Alternatives,” no. GAO-19-629 (September 24, 2019). <https://www.gao.gov/products/GAO-19-629>.

funding.¹⁷ Domestic facilities are required to file such documentation every four years as part of an Animal Welfare Assurance. However, copies of these documents are available to the public only through Freedom of Information Act requests, making large-scale tracking and accountability efforts impossible.

Congress should therefore improve the accuracy and transparency of such information at ARPA-H by requiring that animal information is collected annually and requiring each ARPA-H-funded facility to report the total number of animals per species bred and used by the facility in the previous year, organized by pain and distress category. Congress should also require ARPA-H to create a publicly accessible website for dissemination of this information, including the completed forms.

In addition, Congress should require ARPA-H to implement a system that tracks which agency-funded projects involve the use of animals and that makes this information publicly accessible. The NIH currently collects such information with every grant application using the Research & Related Other Project Information form, which asks applicants to answer “Yes” or “No” to the question “Are Vertebrate Animals Used?”¹⁸ Congress should require ARPA-H to have a similar form and ensure that the answer to that question for each funded project is searchable via a tool comparable to the NIH’s Research Portfolio Online Reporting Tools website, as many other categories of information are.¹⁹

The public holds a necessary and valuable stakeholder perspective and public comments enable accountability. Therefore, Congress should require the ARPA-H director to seek advice from members of the public via public comments during the development of strategic plans and the evaluation of programs and practices. In addition, Congress should require ARPA-H Advisory Committee meetings to be open to the public and allow for public comments. Every NIH Advisory Council and other HHS Advisory Councils (e.g., Advisory Council on Alzheimer’s Research, Care, and Services) hold publicly available meetings to promote transparency and accountability.

Finally, non-federal perspectives will be necessary and valuable to the development of strategic priorities at ARPA-H and in the carrying out of its goals. Every NIH Advisory Council and other HHS Advisory Councils (e.g., Advisory Council on Alzheimer’s Research, Care, and Services) have positions for non-federal members. Congress should therefore require that ARPA-H advisory committee membership includes non-federal representatives, including positions for non-federal subject matter experts in areas of clinical and community research, human-specific methods, and animal protection.

In conclusion, improving the effectiveness and efficiency of medical research, and therefore the health of our entire nation, requires that research funding, policies, and practices keep pace with scientific and technological advances. Human-specific approaches have the potential to transform our understanding of disease risks and mechanisms and to enhance the development of safer and more effective interventions. The Physicians Committee appreciates the Subcommittee’s efforts to advance human-specific methods at ARPA-H to accelerate innovations and transform health breakthroughs. Please do not hesitate to reach out with any questions.

¹⁷ National Institutes of Health. “PHS Policy on Humane Care and Use of Laboratory Animals | OLAW.” Accessed February 7, 2022. <https://olaw.nih.gov/policies-laws/phs-policy.htm>.

¹⁸ National Institutes of Health. “G.220 - R&R Other Project Information Form.” Accessed August 20, 2020.

<https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/general/g.220-r-r-other-project-information-form.htm>.

¹⁹ National Institutes of Health. “RePORTER.” Accessed February 4, 2022. <https://reporter.nih.gov/>.



Statement for the Record
Hearing on "ARPA-H: The Next Frontier of Biomedical Research"
House Committee on Energy and Commerce
February 8, 2022

On behalf of Siemens Healthineers, thank you for holding this important hearing on ARPA-H. As you consider approaches to authorizing this important new program, our company would like to share with the subcommittee some of our recent experiences partnering with the federal government and its network of dedicated grantees to accelerate research concepts into products – not only to maintain our nation's global healthcare innovation leadership, but more important to help every American get access to the right care at the right time. We hope you find them illustrative, and we thank you for your vision and for the drive to bring this program to reality.

Siemens Healthineers is one of the largest healthcare companies and the largest diagnostics company in the world. Our solutions, ranging from laboratory diagnostics (including rapid point of care testing), medical imaging and interventional imaging solutions to radiation therapy, touch 240,000 patients every single hour. In addition to our tests' very high-volume clinical utilization, we are very focused on research to accelerate developments from bench to bedside. For this reason, we are collaborating on over 1,500 active research projects with hundreds of academic medical centers and hospitals across the USA. Additionally, because of our numerous collaborations and the breakthroughs made by our researchers, we can proudly say that as a company, we currently hold over 17,500 patents connected to successful research outcomes.

Historically, the research highlighted above was funded solely by Siemens Healthineers, focusing on product-specific developments; however, we have recently made the decision to bring more focus to government supported research. In conjunction with our academic collaboration partners, we applied for several NIH - National Institute of Biomedical Imaging and Bioengineering (NIBIB) grants, some of which were awarded and are currently active. These grants do not focus on the Siemens-specific development roadmap but do focus on areas that are of broader significance, ones we might not have explored otherwise. Unfortunately, all these projects are in the early stages, targeting basic research. This changed with our joint application for a RADx grant. RADx utilized not only our research strength but placed a heavy focus on our experience of bringing safe and reliable solutions to the market. Bringing a product to the market requires many process steps and most academic institutions, hospitals and/or small organizations do not have the experience in-house.

The following comments will hopefully help in achieving the goal to "drive transformational innovation in health research and speed application and implementation of health breakthroughs:"

- ARPA-H should implement the positive aspects of RADx, such as frequent stakeholder meetings including the FDA, while removing or limiting some constraints such as ultra-quick turnaround timelines that were necessary to combat COVID-19. We believe RADx would have led to additional sustainable solutions if time intervals between milestones would have been slightly longer. The longer intervals should hopefully be acceptable and sufficient to many future projects.
- In the current NIH structure, the majority of Academic Industrial Partnership Grants have an academic prime awardee and an industry sub awardee. Additionally, funding levels are often capped at \$500,000 before indirect costs. While this setup will also work for many ARPA-H grants, one recommendation



would be to have grants that allow companies to focus on topics such as safety, efficacy, regulatory and production. The goal is not to fund industries product roadmap, but to make it intriguing for industry to take a risk. Unfortunately, such projects would require funds north of \$500,000 and in many cases would require industry as prime.

- Based on the outlined “examples of potential projects that ARPA-H could drive,” we could see ARPA-H as a great home for visionary projects such as the scenarios that follow:
- **Health care access, equity, and quality**
 - Every 40 seconds a United State citizen suffers a stroke. Every 4 minutes, someone dies of stroke. Unfortunately, survival rates and outcomes do not only depend on the patient, but it very much depends on where the stroke occurs. In stroke there is the saying, “Time is Brain,” and every minute makes a difference in the long-term effect. Living in close proximity to a comprehensive stroke center might allow a patient to be treated within minutes, where some areas of the country have hours of transportation time - even by helicopter. We are proposing a revolutionary way to treat stroke throughout the country, using endovascular robots at remote hospitals that usually could not treat stroke. The aforementioned robots would allow an expert, highly trained user (e.g neurosurgeon), to perform the procedure from hundreds or even thousands of miles away from the patient. While we will begin working with the FDA rather soon for this remote application, this will be a first in healthcare to bring a highly complex, life-saving procedure closer to the patient. ARPA-H funding would allow Siemens Healthineers to accelerate the work with practitioners, FDA, States Officials, CMS and other payors. ARPA-H would have the potential to bring such lifesaving solutions faster to patients independent of their geographic location.
 - The increased prevalence and acceptance of smart devices and self-testing has created opportunities to significantly impact the management of chronic diseases, from onset to the course of the disease. These devices, such as AI based vitals monitoring, home or self-tests for chronic kidney diseases, women’s health conditions, infectious diseases etc., coupled with population health data have given us the ability to envisage a healthcare system where individuals can be monitored far more precisely for their risk in developing chronic conditions. And consequently, delay onset of more severe conditions such as End Stage Renal Disease, significantly improving quality of life. In our more connected world this enables bringing prevention and management of disease anywhere in the community irrespective of distance from a clinician. A similar approach on episodic events is also highly impactful, for example a diagnosis of AMI at the point of occurrence dramatically reduces time to diagnosis and intervention and therefore, potential for recovery and reduces ER crowding. Siemens Healthineers is at the forefront of developing an infrastructure and integrated solutions to enable seamless integration of information across these settings – from the home, to an outpatient setting through to a hospital. ARPA-H funding would greatly accelerate this development, which we strongly believe will have a tremendous benefit in keeping people



healthy independent of access to healthcare and reduce the overall burden on the healthcare systems.

- **Cancer and other chronic diseases**

- The knowledge gap between Comprehensive Cancer Centers and a non-specialized hospital where cancer treatment is limited to chemo- and radiation therapy is significant. We have been working on a pathway companion approach that pulls all the relevant information about the patient from the electronic medical record and integrates this data using smart logic. This logic will provide information about potential treatment options that go beyond chemo- and radiation therapy. Tools such as this have the potential to inform local physicians about advanced treatment options such as CAR T Cell Therapy or Proton Therapy. ARPA-H could support further standardization of such integrated diagnostics tools to ensure that all patients and practitioners are aware of all applicable treatment options.
- Currently, Radiation or Proton Therapy are lifesaving treatments that require multiple patient visits over weeks or months and have significant side effects. A potential new technology called FLASH might have the ability to bundle this lengthy treatment in a sub-second long one-time treatment. Aside from the convenience, the approach holds the promise to significantly reduce side effects of the treatment. One of the reasons is that blood will have very, very little exposure to radiation, unlike in the current method. ARPA-H could significantly accelerate the introduction of this revolutionary treatment, when compared to normal industry product development process.

- **Infectious disease**

- Our recent experiences with SARS-COV-2 have demonstrated the critical need for a comprehensive response strategy for infectious disease screening to monitor and control spread of infection – allowing treatments and vaccines to be effectively developed. This involves testing at all levels – from self-test, to decentralized settings to central laboratories – as well as an intelligent monitoring system using AI to identify areas of concern, increase testing by rapid deployment of tests and provide reporting to monitor the infection. Through internal development, access to partners, informatics tools and use of our AI companion pathway, Healthineers is uniquely poised to realize such a solution. Through our global reach, we are able to deliver a robust supply chain strategy, as well as adapt to evolving variants or testing requirements in a timely manner, and with rigor.

As an organization, we are highly motivated by opportunities that allow us to engage in innovative research. We excel at providing tailored solutions to support routine cases to complex treatments. Our portfolio boasts both expertise and experience that can bridge the clinical and technical divide. Given these capabilities and the qualifications mentioned above, we would like to express our interest in assisting with the development of this program, specifically as it relates to contract structure. We recognize the value and importance of having an industry representative serve in this capacity to ensure all perspectives are included and taken into consideration.



On behalf of Siemens Healthineers, we would like to thank you again for the opportunity to comment on this very important initiative. ARPA-H has the potential to change the pace of developments and distribution of healthcare and this initiative has our strong support. Please let us know if we can assist in the development of ARPA-H.

Best regards,

A handwritten signature in black ink, appearing to read "C. Eusemann".

Christian Eusemann, PhD
VP Research & Innovation
Collaboration Officer

WHAT IS CHINA'S THOUSAND TALENTS PLAN?

The nation's bid to lure back ex-pat scientists and recruit highly-skilled foreign researchers is now in its tenth year.

BY HEPENG JIA

In 2008, China's central government announced the Thousand Talents Plan: a scheme to bring leading Chinese scientists, academics and entrepreneurs living abroad back to China. In 2011, the scheme grew to encompass younger talent and foreign scientists, and a decade later, the Thousand Talents Plan has attracted more than 7,000 people overall. For Chinese scientists, the scheme has given them a strong financial incentive to return home. For foreigners, it's an opportunity to join the Chinese system with major administrative hurdles removed.

How does it work?

Previous programmes to lure back ex-pat scientists elevated postdocs and junior faculty members to full professorial or equivalent positions in China, but the Thousand Talents Plan was more ambitious, aiming to target professors and chief scientists in the West. This approach led to tougher recruitment criteria across all schemes, and high-level positions became less easy to come by. It's well understood in the research community that scientists recruited through talent schemes

will gain access to much higher salaries and research funding levels than their locally trained peers.

Where do I begin?

To apply for any of the Thousand Talents schemes, you must already have a firm job offer from a Chinese institution. If you are a full professor at a leading Western university, you will more than likely be eligible for a place on the Thousand Talents scheme for senior academics, as long as your research record meets the demands of your field of study in China. The scheme is open to Chinese scientists under 55 years of age, and foreigners younger than 65. All applicants must have worked at renowned universities outside China, and have a strong publication record.

When you've confirmed a position with a Chinese institution, your university will probably suggest that you apply for the Thousand Talents programme, and ask for your CV with a list of published papers, copies of all academic qualifications (original or certified) and full-text copies of your highest impact research papers. Usually, letters of reference are not required. The university will then apply on your behalf. The length of the application process (which includes an interview) can be a matter of months if the applicant meets all of the criteria first time around. However, after signing their employment contract and agreeing to the terms of the Thousand Talents Plan, such as a minimum three to five years of working in China, scientists may need to wait for all aspects of their agreed research project to be realized, as not every financial and administrative decision is controlled directly by the university.

What are the benefits?

All successful applicants can expect a 1 million yuan (US\$151,000) starting bonus, and the opportunity to apply for a research fund of 3–5 million yuan. Foreign scientists receive additional incentives, such as accommodation subsidies, meal allowances, relocation compensation, paid-for visits home and subsidized education costs. Employers are also obliged to find jobs

for foreign spouses, or provide an equivalent local salary. In addition, the Thousand Youth Talents Plan targets foreign and ex-pat Chinese scientists under the age of 40 — unlike the main Thousand Talents Plan, Chinese returnees receive the same benefits as foreign recruits under the Thousand Youth Talents Plan. More details for all programmes can be found on the official website, 1000plan.org/en/.

“YOU MUST ALREADY HAVE A FIRM JOB OFFER.”

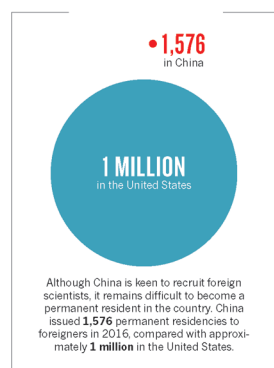
Whether you were born in China or come from abroad, all applications to the Thousand Talents scheme go through your Chinese university employer. Only one institution can apply on your behalf, so you cannot make multiple applications.

What makes for a successful Thousand Talents application?

Your publication record, career record and communication skills are all important. Chinese institutions pay the greatest attention to the number of high-impact papers published. They also prefer scientists who have graduated from leading universities. Finally, make sure you establish the value you can add to your chosen research institution in China, highlighting your research ideas and particular areas of expertise.

A common mistake is to focus on one's own research without thinking about the department or school's research conditions and directions. Another is to stress the significance of your work, rather than how it could attract funding or when it could be published. In China, it is expected that newly employed scientists will be productive as quickly as possible. Creativity and originality are not valued as highly as publication rate. ■

Hepeng Jia is a science writer in Beijing and Ithaca, New York.



Attachment—Additional Questions for the Record

**Subcommittee on Health
Hearing on
"ARPA-H: The Next Frontier of Biomedical Research"
February 8, 2022**

Esther Krofah, Executive Director, FasterCures and Center for Public Health at the Milken Institute

The Honorable Frank Pallone, Jr. (D-NJ)

1. The incredible relief provided by COVID-19 vaccines and treatments that were made possible by biomedical innovation are a testament to the importance of strengthening the biomedical ecosystem to support future medical breakthroughs.

- a. How do you see ARPA-H playing a role in improving our nation's pandemic preparedness? Are there any particular technologies or platforms that could lead to breakthroughs in our ability to prevent or respond to novel threats?

While ARPA-H's mission should be broader than pandemic preparedness, it would be ideally situated to leverage learnings from the COVID-19 pandemic and prioritize investments that will both leave us better prepared for future public health emergencies and benefit the overall biomedical innovation ecosystem.

- Investment should be prioritized in platform technologies (e.g., mRNA, prototype pathogens) and research infrastructure. COVID 19 shone a spotlight on the challenges in our clinical trial infrastructure, particularly the lack of ability to engage community-level providers that enable greater patient participation and those impacted disproportionately by the burden of disease. ARPA-H offers an opportunity to build an infrastructure platform to support a national community-based clinical trial network.
 - A number of high-value platforms and assets were created during the pandemic that should be sustained and made available to ARPA-H (e.g., RADx, the National COVID Cohort Collaborative data platform, NIH's Clinical Trial Capacity Inventory).
 - Collaboration, across and within sectors, was key to accelerating research and product development during the pandemic, and ARPA-H should be a platform for continued collaboration among those players.
 - b. How do you envision ARPA-H working in a collaborative manner with other research agencies?

A multi-agency and multi-stakeholder approach should be employed for setting priorities and guiding/informing projects. First, ARPA-H must ensure its work is complementary to and not duplicative of other science-funding agencies such as

DARPA, NSF, and BARDA. Second, we strongly believe that representatives of patients, including those from underserved communities, must be part of priority-setting, defining the problems most important to be solved. And finally, if ARPA-H's work is to be truly solutions-oriented, it must be actively and regularly engaged with and informed by other agencies critical to advancing solutions to patients, such as FDA and CMS.

- c. In what ways can ARPA-H amplify the important work done across HHS and other federal entities working to improve health?

ARPA-H should work in close coordination with other science-funding agencies to ensure its work is not duplicative but rather addresses the types of cross-cutting challenges that other agencies cannot. Because of its focus on problem-solving and commercialization of products, it should have a strong interest in close coordination with regulatory and reimbursement agencies like FDA and CMS to ensure that the projects it funds reach their intended end-users.

- d. What metrics should be used to assess the progress of ARPA-H?

In the near term, we should be looking at the agency's ability to organize quickly; attract the type of leadership and program managers who are a key to DARPA's success; get needed and appropriate authorities in place to enable its rapid and flexible operations; and prioritize problems in areas of high unmet need and low investment, to be addressed in consultation with a multi-agency, multi-stakeholder advisory group.

An important ingredient in DARPA's success is the ability to "fail fast," and failure for technical reasons is not viewed as a negative. This culture must be replicated at ARPA-H, and any metrics utilized must not create unintended consequences of penalizing "failure."

In the medium- to long term, therefore, ARPA-H should be evaluated by its ability to stimulate the development and commercialization of products and platforms that benefit the biomedical innovation ecosystem and ultimately patients—or to fail fast and apply the lessons learned to new approaches.

We also need to ensure the projects selected by ARPA-H improve the lives of populations that are historically underserved and come from marginalized minority communities.

- 2. When we consider DARPA, the model agency for ARPA-H, it is a unique agency that benefits from numerous special authorities. For example, DARPA is able to capitalize on flexible hiring and procurement authorities, including grants, contracts, cooperative agreements and other transaction authorities. These special authorities have in part paved the way for DARPA's success.
 - a. In scenarios where ARPA-H is working with prototype technologies or companies that don't typically partner with the government, what special authorities are needed to ensure successful development of new platform technologies?

ARPA-H would certainly require Other Transaction Authority, which gives it flexibility in the contracting and procurement contracting process. It needs to have a strong focus on technology transfer and commercialization—though that would not necessarily require different authorities, just skills and prioritization. It would also require freedom from federal hiring constraints to attract the types of personnel required to manage these projects and pay them competitively.

- b. How can the government ensure that technologies developed through the ARPA-H pipeline make it into the mainstream and are accessible to all who need them?

The private sector is a critical partner in this work, whether as collaborators in executing specific projects or as the recipients and amplifiers of any innovation coming out of the program. Technology transfer and commercialization will be central considerations in the policies and approach of the new agency.

Another aspect of working with the private sector could be finding ways to leverage private investment in technologies that might come out of ARPA-H. BARDA Ventures could be a potential model in this regard, or In-Q-Tel, which invests in new technologies related to national security.

3. ARPA-H would employ a high-risk, high-reward and fail fast model. ARPA-H would also collaborate with the private sector and other stakeholders to ensure that the projects it supports ultimately lead to improvements in health for patients.

- a. From your perspective, what would the collaboration between ARPA-H and the private sector and other stakeholders look like?

As noted above, the private sector is a critical partner in ARPA-H's work, whether directly contracted to execute specific projects or through licensing intellectual property created at academic institutions in pursuit of its goals. Innovative products do not make it to patients without the involvement of the private sector.

We believe that ARPA-H should have a collaborative priority-setting process that involves a multi-stakeholder advisory group, including representatives of patients, to ensure that the agency is aiming its efforts at solving problems in areas of high unmet need with low investment.

The Honorable Bobby L. Rush (D-IL)

1. Last May, I was proud to introduce the LOANS for Biomedical Research Act (H.R. 3437), which would establish a BioBonds Program. The BioBonds Program is a novel approach to fund biomedical research by leveraging the significant, untapped resources of private-sector institutional investors, including pension funds.

BioBonds are a package of loans made to researchers at eligible biomedical companies and universities. Banks would package these loans and then sell them to institutional investors. BioBonds are similar in structure to green bonds, which generate hundreds of

billions of dollars in investments for climate and environmental projects. In 2020, the green bond market reached \$1 trillion dollars. Investments generated by BioBonds would help advance translational research and enable promising research to progress from the lab to the patient.

In my opinion, BioBonds fits squarely in the overall directive of ARPA-H to use funds to translate scientific discoveries into technological innovations. This innovative financing mechanism is consistent with the goals and authorizing legislation for ARPA-H and could enable meaningful advancements in a wide range of diseases. To say it another way, I believe a BioBonds program, like the one established in my bill, could be operationalized within ARPA-H.

- a. Ms. Krofah: Do you agree that BioBonds fit into the fast-growing ESG (or Environmental, Social, Governance) arena in which investors look not only at return, but also at public welfare, as is the case with green bonds? Why or why not?

We agree that the BioBonds proposal for debt financing is a valuable addition to the array of options available to support biomedical innovation, engaging a broader range of investor types. In our view, this seems to fit squarely into the current interest in investing in companies that create value across the ESG spectrum. We would like to see more focus on the "Social" elements, and specifically the health-related benefits, tracked by ESG metrics. We are looking at how the Milken Institute might play a role in defining such metrics and driving their adoption.

Attachment—Additional Questions for the Record

Subcommittee on Health
Hearing on
"ARPA-H: The Next Frontier of Biomedical Research"
February 8, 2022

Geoffrey Ling, M.D., Ph.D., COL (ret), Chief Executive Officer, On Demand
Pharmaceuticals

The Honorable Frank Pallone, Jr. (D-NJ)

1. *Part of the proposed mission of ARPA-H is "to make pivotal investments in breakthrough technologies and broadly applicable platforms, capabilities, resources, and solutions that have the potential to transform important areas of medicine and health."*

This is a broad mission, but the Administration has identified specific examples of projects that ARPA-H is well suited to explore, such as "the development of accurate, wearable, blood pressure technology; the preparation of mRNA vaccines against common forms of cancer, and drug or gene therapy delivery systems that can target any organ, tissue, or cell type."

- a. *Could you provide some examples of platforms or technologies that have enabled transformative progress in biomedical research?*

Indeed, platform technologies underlie the most important advances in medicine. These technological advances leverage discoveries made through basic and clinical research to drive new treatments and cures for human diseases and disorders. This is why the majority of Nobel prizes are awarded for the development of new technologies. Examples include the Moderna mRNA vaccine against COVID-19 (Originally funded in 2010 by DARPA). mRNA technology will eventually lead to vaccines against other infections including herpes and malaria, improved flu vaccines, and, if necessary, updated coronavirus vaccinations. Others include targeted cancer therapies, robot-assisted surgery, the use of artificial intelligence to detect sepsis, the MRI machine and, of course, the internet (ARPAnet, 1963).

- b. *Can you provide examples of breakthrough technologies that draw from atypical disciplines and talk about why the flexibility envisioned by the ARPA-H model is important?*

There are a host of examples, but to name a few: autonomous vehicles, 3D printing, stealth technologies, bioprinting, wearable and smart home technologies, and drones all drew from atypical disciplines to make advances that have fundamentally changed the world.

The key to the success of ARPA-H will be operating on the same nimble program model that DARPA has used for decades to advance technologies that draw from atypical disciplines. Had any of the aforementioned technologies solely relied on traditional grant programs used by other Federal agencies, we would not have seen them come to market at the pace they did. Nimble and flexible program decision making by skilled program managers is key to success because it allows them to pivot based on experience and dedicate dollars towards the most promising approaches rather than sticking with bets that are not panning out. For example, if ARPA-H was to rely on traditional peer reviewed granting mechanisms, review committees would rarely provide funding for high-risk high-reward projects necessary to swing for the fences. Instead, we would see incremental progress stretched over many more years. These funding mechanisms are great for discovery-based research that build slowly on the advances of others but are not well suited for invention and creation of new capabilities.

2. *There is an ongoing and healthy debate on the appropriate placement of ARPA-H. Generally, there is a consensus that ARPA-H will need an independent structure and novel culture, compared to traditional NIH Institutes and Centers, to deliver innovative ideas in health and medicine. After all, the success of DARPA, the model for ARPA-H, is in part due to its independent structure and innovative culture.*

a. *In your testimony, you discuss the importance of independence for ARPA-H. What do you mean by that?*

Independence is essential to the success of ARPA-H. When President Eisenhower established DARPA, he was under pressure from the Departments of Army and Navy to place the agency inside one of those structures to avoid duplication of administrative, legal and operational functions. He resisted this pressure, recognizing that such institutional constraints would run counter to the core principles of DARPA's modus operandi: a culture of urgency, innovation and efficiency. Arguably, it was the most consequential decision Eisenhower made in setting DARPA up for success. His rationale and Congress' support for that decision are as important to ARPA-H's success as the rest of the DARPA model.

The inability of the *NIH Common Fund* and the *National Center for Advancing Translational Research* to reach their potential and yield life-saving innovations are the best examples of how unrealistic it is to locate a new priority initiative within the NIH – the largest biomedical research agency in the world – with the expectation it will operate with “independence” and “its own culture.” With nearly \$1B in annual budget and stated funding criteria for programs that are “Transformative, Catalytic, Synergistic, Cross-cutting and Unique,” the *Common Fund* has not made progress in the development of technologies or capabilities that address critical gaps in diagnostics, therapeutics and curative treatments. Further, NCATS has been bogged down with bureaucratic burden that has limited their ability to use other transactional authorities with the kind of speed and efficiency required to drive rapid innovation.

It is not just about the research. At the very beginning of a project, DARPA demands that its performers address how they will transition their technology. Important

questions must be identified and addressed up front such as (1) regulatory strategy, (2) commercialization approach – who will make this, who will distribute it, who will service it and (3) how will providers and patients adopt it?

b. If ARPA-H is placed at NIH, would it be able to develop a distinct culture?

Placing ARPA-H within the NIH sends a message that this new agency is merely more of the same, with a different name and some new funding. ARPA-H must be free to develop its own culture of innovation, with its focus on getting advancements out of labs and into patients. The purpose of having ARPA-H independent of the NIH is to remove it from NIH bureaucracy. Placing ARPA-H in the NIH potentially subjects it to slow processes that are not designed for the purpose of running a DARPA-like agency. Operationally, ARPA-H needs the ability to eliminate bureaucratic processes so funds can be efficiently distributed to performers with the rigorous funding oversight and accountability that is a hallmark of DARPA's culture. Without this independence, ARPA-H would be subsumed by the NIH.

Additionally, it is important to note that DARPA doesn't own or operate its own research labs. It oversees and manages research conducted at universities, government labs, established industry R&D facilities and start-up companies. Notably, it is often the start-ups that innovate and work at the pace and focus needed to achieve meaningful timely advances in clinical care. For ARPA-H to succeed, industry must be highly engaged. The processes of manufacturing and distribution are critical to advancing these innovations into the clinical setting at facilities across the country. To facilitate this type of effort, ARPA-H should be independent and free.

c. How do we ensure accountability and transparency while also providing for this autonomy and independence that is so important to the success of ARPA-H?

Accountability and transparency need to be embedded in the operating policies and structure of the Agency, just as they are for DARPA. ARPA-H program managers must have control and responsibility for their projects and their performers. At DARPA, there is a contract clause that gives the government full rights to terminate funding for any reason without prior notice. This ensures that the performers execute their milestones within budget and on time. Additionally, DARPA typically executes milestone payable contracts. This means that the performers are not paid until they successfully achieve goals, which further ensures accountability.

ARPA-H must be accountable and transparent with the Congress as well. Because each program will have clear contractual milestones, timelines and budget, the Congress should be able to gauge each and every program's progress and success in real time. This kind of transparency and accountability is unheard of in the NIH world.

3. *Two key actors within DARPA, the model for ARPA-H, are the Director and program managers. Generally, the responsibility of the Director is to approve funding and programs, while program managers are expected to oversee project execution and performance. The Biden Administration's proposed structure for ARPA-H also includes a Director and program managers.*

- a. *Finding the right inaugural Director for ARPA-H will be critical to building a distinct culture and ultimately ensuring its success. What do you see as the key qualities for this individual? What type of track record and qualifications should they have and how will those be helpful in leading ARPA-H?*

The inaugural Director for ARPA-H must be an established leader with a track record of success using nimble contract-based models for research funding. Most importantly, the candidate must lead with the attitude and principles at the core of ARPA-H: innovation, efficiency, and accountability. The Director's ability to inspire inaugural program managers and all players in the ecosystem is essential. I believe that looking to an individual with previous experience at DARPA is a solid starting point for the new agency.

It is logical that if ARPA-H is modeled on DARPA that the inaugural leader would have senior DARPA leadership experience. Other qualifications should include a doctorate (PhD) in a technical area and, optionally, medical training (MD or DO). The Director must have experience in both government and private sector, with previous organizational leadership experience at equivalent levels to the ARPA-H Director. Background and strong working knowledge of the FDA regulatory process is also critical since many of the medical interventions developed through ARPA-H funding will be headed to regulatory review and should be designed and tested with that in mind. They should also have familiarity with medical product manufacturing and distribution, as well as clinical care operations to ensure that they have a firm understanding of the barriers to adoption by providers and patients.

- b. *The Director will need to be surrounded by the right team of program managers. What qualities are important for these program managers? How will ARPA-H recruit and retain these talented individuals?*

Under exceptional leadership, ARPA-H should attract the highest quality talent. DARPA's reputation as "the gold standard of innovation" will serve this agency's recruiting efforts if the leadership model and operating structure are the same. Program managers need to have deep experience leading teams (ideally across multiple disciplines), operating with accountability, meeting deliverables, and executing projects on time and on budget. They must be resilient and open-minded. For that reason, DARPA, and thus ARPA-H should be constantly recruiting new talent because it takes a special individual with an unusual set of skills, knowledge, and creativity to succeed in these roles. It is not just a matter of bringing in smart people.

- c. *Can you talk about the diversity of scientific disciplines and backgrounds that program managers will need to approach health in new ways?*

Program Managers are talented and innovative thinkers who come from a broad range of backgrounds. ARPA-H program managers will necessarily have to have diverse expertise because the problems they will be tackling require a diverse set of approaches. For that reason, we are going to want people with backgrounds that range from medicine, to medical device experts, to data scientists, PH.D. biologists, physicists, engineers, chemists, mathematicians, social scientists, psychologists and technologists. The diversity of program directors must reflect the diversity of challenges that they are going to attack.

4. *The Office of Science and Technology Policy (OSTP) and NIH held a series of fifteen listening sessions with stakeholders across the biomedical ecosystem to seek input on ARPA-H. More than 5,000 individuals registered for these sessions, providing nearly 1,000 suggestions, ideas, and questions across the 15 sessions*

- a. *What input can or should stakeholders have in the selection of ARPA-H projects?*

One of the most critical distinctions between DARPA and the NIH is the process for project selection. Following the DARPA model, ARPA-H will not solicit ideas for funding the way NIH operates and funds proposals. Projects will be defined by "Solving for X." -- Identifying a gap in a capability (whose innovation could have broad application) and solving for it. ARPA-H will not focus on disease specific issues, but rather will identify what capability could be built that addresses the greatest challenges. The investments made by ARPA-H should reflect real healthcare needs and technological opportunity to address them.

- b. *How should that input be incorporated and by who?*

5. *Since DARPA is considered to be the model for ARPA-H, it might be helpful to hear more about its budget while keeping in mind that biomedical research tends to be expensive relative to other areas of technology R&D.*

- a. *Can you shed light on DARPA's operating budget? Are you aware of DARPA displacing any funds from other existing DoD capacities?*

DARPA's operating budget is about 4% of the total DoD research and development (R&D budget). DARPA's annual budget has remained relatively steady. The President's FY2022 budget request for DARPA is \$3.528 billion. The FY2021 enacted budget was \$3.500 billion. DARPA-funded research has made important science and technology contributions that have led to the development of both military and commercial technologies, such as precision guided missiles, stealth, the internet, and personal electronics. Nearly all of DARPA's funding falls under the budget categories of basic research, applied research, and advanced technology development 6.1, 6.2, and 6.3.

Commented [M51]: This number is not correct. Is it .8%?

Funding under these categories is referred to by DoD as the science and technology (S&T) and research and development (R&D) budget.

DARPA is a separate line item in the President's DoD Budget that is proposed to the Congress every year. To my knowledge, I am unaware of DARPA displacing any funds from any other existing DoD capacities.

b. Do you think the Biden's Administration's proposal of \$6.5 billion over three years is an appropriate figure?

Yes, I think that President Biden's proposed \$6.5 billion over 3 years is an appropriate figure. DARPA's budget of \$3.5 billion is relatively small compared to the total DoD R&D budget of \$112 Billion. This funding ratio should exist for ARPA-H vis a vis the total HHS R&D budget. Once ARPA-H is well established, the congress will want to grow it substantially. Each dollar spent at ARPA-H, if it is functioning independently from the NIH, is a healthcare and economic bargain because the return on investment for the public will dwarf the expenditures.

6. The ARPA-H proposal put forth by the Biden Administration identifies the Defense Advanced Research Projects Agency, or DARPA, as the model for ARPA-H. Since its founding in 1958, DARPA has supported crucial technological advancements in the interest of national security. And as you noted in your testimony, DARPA is the gold standard for innovation.

a. Having served at DARPA for 11 years, could you help the Committee understand what you see as the key aspects of DARPA culture that made it successful?

The key aspects of DARPA's culture that makes it successful are (1) risk taking attitude, (2) program manager empowerment, (3) strict oversight and accountability and (4) milestone driven timeline limited process of R&D execution, and (5) complete independence from traditional DoD bureaucracy.

A critical element of the DARPA culture is attention to the Heilmeier catechism. Dr. Heilmeier was a DARPA Director who developed a series of questions that every PM had to address when developing each new program. The Heilmeier catechism is: (1) What are you trying to do? Articulate your objectives using absolutely no jargon, (2) How is it done today, and what are the limits of current practice? (3) What is new in your approach and why do you think it will be successful? (4) Who cares? (5) If you are successful, what difference will it make? (6) What are the risks? (7) How much will it cost? (8) How long will it take? and (9) What are the mid-term and final "exams" to check for success?

Risk-taking culture. At DARPA, the culture is not only about risk taking but how that risk is managed. DARPA has a culture of risk-taking and tolerance for failure that

encourages radical innovation to solve a problem. DARPA focuses on high-risk, high-reward research. The goal is to discover how far the American scientific community can go. When a performer is unable to achieve a desired outcome, it is typically because the limits of current knowledge have been met. So by "failure" there has been important success: where the limit is and how to go beyond it. It is common knowledge that failure is often the best teacher. Risk is managed by the DARPA process itself, which at its heart is the program manager.

Program manager (PM) empowerment. The DARPA model is characterized by a flat organization that empowers its tenure-limited PMs with trust, autonomy, and the ability to take risks on innovative ideas. The PM is the source of the program idea. It is the PM who is responsible for program execution. It is the PM who has authority to "hire and fire" and to reallocate funding so as to ensure that the program is completed in an efficient and timely manner.

Congress has aided DARPA's efforts by granting the agency certain flexible acquisition and personnel hiring authorities, which have allowed DARPA to engage with people and entities that may have otherwise been reluctant to interact and do business with DOD. This model allows DARPA to avoid internal processes and rules that slow action in other federal agencies.

Since tenure is limited for each program manager, they have an impatience to accomplish their program's goals while they are still at the Agency. This ensures timely execution of the work by the performers.

Program managers play a key role in the technical direction of each project. Unlike most program managers in federal R&D agencies, DARPA program managers are tasked with creating new programs and projects and quickly funding innovative ideas. DARPA program managers are responsible for project selection and, if milestones aren't met, the termination of a project. In contrast, program managers from other federal programs such as NSF and NIH inherit existing programs and select projects based primarily on the peer review rankings.

Strict oversight. Because every program has clearly identified milestones and is on a strict timeline, program managers and the Congress can ascertain how well each program is progressing – in real time. The PMs typically meet remotely with performers on a weekly basis, in person every month, and have formal reviews quarterly.

Milestone driven and timeline limited process. DARPA awards contracts to performers. These contracts have mutually agreed upon milestones and timelines for the work. DARPA's culture is to adequately resource performers so they can execute the work in as short a time as possible. Of all resources, time is the most precious and is thus the one resource to be used sparingly.

Independence from DOD bureaucracy. If DARPA was part of the traditional DOD decision making bureaucracy, it would fall apart. It is independence from troublesome bureaucracy that allows the agency to remain nimble and take risks.

- b. *How can ARPA-H apply those lessons to its distinct health-focused mission?*

DARPA attributes its long history of successful innovation to four factors: (1) Trust and autonomy; (2) Limited tenure and the urgency it promotes; (3) A sense of mission; and (4) Risk-taking and tolerance for failure. ARPA-H can apply these same factors to address critical health system issues that other Federal agencies cannot due to the nature of their funding mechanisms, investment management strategies, and major institutional and cultural barriers.

c. *How would ARPA-H need to differ from DARPA and why?*

DARPA is responsible for catalyzing the development of technologies that maintain and advance the capabilities and technical superiority of the U.S. military. ARPA-H will achieve **medical breakthroughs** by building new platform technologies to support research that directly affirms, refutes, or otherwise changes current clinical practice. Like DARPA, it would do this using milestone-driven, time-limited contracts as the central mechanism for driving innovation. The main difference is in the mission and focus of the agency. ARPA-H will transform healthcare and medicine as we know it, the same way that DARPA transformed the way we fight wars.

7. *In your testimony, you talked about how the Administration would evaluate ARPA-H.*

a. *Based on your experience at DARPA, what metrics should be used to assess the progress of ARPA-H?*

DARPA has maximum control over the conduct of its programs. Program Managers meet with performers regularly, sometimes weekly. Performers are often placed on a milestone-based contract where they must meet each milestone to be paid. The program funds are paid out incrementally with demonstrated success. DARPA contracts state that the government may terminate the contract at any time without prior notice and at the government's discretion, meaning failure to perform can result in termination of contract. Because the Administration has decided to place ARPA-H into the NIH structure, ARPA-H independence is at serious risk. The Congress should look carefully at the make-up of its program managers, time for decision making, time for contract implementation, time for execution of Broad Agency Announcements, etc. Since the agency has been placed within a massive bureaucracy, the Congress will want to make sure that it does not succumb to it.

b. *Additionally, what regulatory agencies or processes are best positioned to evaluate this progress and success?*

It is critical that ARPA-H evaluates the progress and success of each program regularly. At DARPA, the Office Directors meet with each program manager on a quarterly basis and the Agency Director on an annual basis.

Other government agencies are included in reviews. For example, while serving at DARPA, my Revolutionizing Prosthetics program routinely included federal officers from FDA, NIH, VA and NSF at proposal selection and then every quarterly review thereafter. By involving these federal agencies, the program was able to execute more efficiently and deliver the most advanced prosthetic arm/hand to patients in history. In fact, the

prosthetic arm entered clinical trials with the VA collaboration within 2 years, submitted the required new device application for FDA review in 4 years and received full FDA approval by 8 years. We should expect the same efficiency and collaboration of ARPA-H.

The Honorable Tony Cárdenas (D-CA)

1. *ARPA-H is meant to drive transformational innovation in health research and speed application and implementation of health breakthroughs. Emerging human-specific 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. Despite the biomedical advancements arising from human-specific innovations, these methods are not prioritized agency-wide. It is also known that animal studies have serious problems in translating to effective health breakthroughs. How might leadership at ARPA-H ensure strategic focus and funding for the development and use of advanced human-specific research approaches to reach the medical breakthroughs we need?*

I will use an example to answer Congressman Cardenas's question. A potential candidate ARPA-H program will be new medical imaging technology.

In 1972, the first CT scanner was made available. In 1977, the MRI scanner was introduced. Since then 45 years later, we have not had another equivalent advancement in medical imaging. Although clinically useful, the current MRI is based on a high strength magnet. That magnet in turn requires a superconducting quantum interference device (SQUID) and thus has high energy requirements and need for specially shielded rooms. This is of course very expensive. Finally, the limit of resolution of 0.8 X 0.8 X 1.6mm for a 1.5T MRI. For reference a cancer cell is 0.001mm.

ARPA-H's objective would be the development of the next-generation medical imaging to have better diagnostic capabilities, be small and lighter, more energy efficient and cost less.

Image resolution and processing could be dramatically improved through a combination of:

- 1) Application of different physics instead of using superconducting magnets and
- 2) Advanced signal processing algorithms coupled with AI (artificial intelligence) to increase scan speed and diagnostic accuracy

The ARPA-H process is modeled on DARPA's process. ARPA-H would follow the DARPA project selection and management process and, in particular as noted above, follow the Heilmeier Catechism. For the advanced imaging diagnostic program, the catechism would be applied as follows:

1) What are you trying to do? Articulate your objectives using absolutely no jargon.

Develop a diagnostic imaging system that detects disease at the earliest stage of development. It will achieve this by having image resolution that is at least 2-3 orders of magnitude superior to MRI, i.e. allow pathology to be detected when it is very early and very small. This new system will be smaller in size, less expensive and more energy efficient than current MRI systems. Finally, it will use technology that is low-risk to patients.

2) How is it done today, and what are the limits of current practice?

MRI technology relies on a very strong magnet to hyperpolarize the hydrogen ions in the patient's body. The image is created by the different orientations the hydrogen ions take when exposed to the magnetic field. However, using a strong magnetic field for medical imaging is inefficient. A very strong magnet is required, which must be supercooled. As a result, MRIs are cumbersome, costly and require tremendous energy.

The most common clinical magnet used in hospitals is 1.5T, generating a magnetic field that is 1.5 times the strength of Earth's gravitational field. Engineers and doctors now use 7T magnets and greater to capture better images. Due to the inherent inefficiency of using magnetic fields, the performance of these large magnets is only marginally better for detecting smaller disease states. The technology has reached its limit.

3) What's new in your approach and why do you think it will be successful?

Apply an entirely different type of physics for medical imaging. Leading options include:

- Quantum Orbital Resonance Spectroscopy (QORS) is a promising physics area to hyperpolarize hydrogen ions. In laboratory studies, QORS has been shown to hyperpolarize hydrogen ions at an efficiency that is 100X better than a magnetic field. It does not require super cooling.
- Ultrasound and Near Infrared (IR) with Compression Imaging combines older techniques with a few novel improvements. Light is scattered when it is transmitted into the body. By coupling this with ultrasound and using time reversed light, the light and sound energies can be optically focused on specific body areas to be studied. Then, new compression imaging techniques can be used. Compression imaging works better when information is sparser and scrambled, making the scattered light of body tissue ideal for measurement. Compression imaging uses these features in a way that reduces the number of required measurements, thus achieving a much greater resolution.

4) Who cares?

According to the Centers for Medicare & Medicaid Services (CMS), the National Health Expenditure grew 3.9% to \$3.5 trillion in 2017 and accounted for 17.9% of Gross Domestic Product (GDP). Everyone cares about saving lives and saving money. Beneficiaries of advanced imaging diagnostics would include patients, doctors, insurance companies, pharmaceutical companies and CMS/the U.S. Government, who stands to gain the most.

5) If you're successful, what difference will it make?

An imaging system with greater resolution, that is smaller, lighter and less-expensive than the current MRI will result in: Earlier detection of diseases like cancer and atherosclerosis greatly improving the chances of existing therapies to work; Greater access for small clinics, rural and critical access hospitals and combat zones; Lower operating and patient costs. The cost differential between early and late stage detection of disease supports strengthening our investment in diagnostic programs for early disease detection. Treating advanced versus early-stage breast cancer, for example, is associated with a higher death rate and significant cost increases. In a 2019 analysis, the average costs per patient allowed by the insurance company in the year after diagnosis were \$60,637, \$82,121, \$129,387 and \$134,662 for disease stage 0, I/II, III, and IV, respectively. The survival rate for women with stage 0 or stage I breast cancer is close to 100% but drops to just 22% once the cancer metastasizes.

6) What are the risks and payoffs?

The technical risks involved are related to the maturity of the science. A great deal of the physics is understood, but its application to medical imaging is not. The scientific rationale underpinning the various physics approaches will need to be carefully considered. The physicists and technologists working in this space primarily use these techniques for non-medical purposes. Thus, a new community of scholars will need to be formed. From a financial standpoint, this will be disruptive to the current business model of large MRI manufacturers and providers. Finally, there is the opportunity cost if this is not pursued. The benefits are clear. The impact to society is immense.

7) How much will it cost?

Time is the most expensive resource. To mitigate this, sufficient resources must be made available to the performers. A well-managed program will cost about \$50-100M over a 4-year period. There must be close supervision by an expert government team working across the technological and medical communities as well. This team will work across government agencies to include DOE, FDA, NIH, NSL, NIST and CMS.

8) How long will it take?

Program execution should be 4 years: Three phases, spanning 4 years, with clear deliverables in each phase. An aggressive timeline with clear milestones and metrics for both success and failure will be required.

9) What are the midterm and final "exams" to check for success?

"Go" and "No-Go" phases can run simultaneously:

Phase 1: Explore and validate potential candidate approaches.

- Duration: 18 months
- Three Technical Goals Need to be Met:
 - (1) Investigate non-traditional approaches for high resolution local and low resolution global functional imaging, and high resolution structural imaging;
 - (2) Demonstrate spatiotemporal resolution and imaging depth and FOV compatible with focus area;
 - (3) Include concepts to stitch together images at different scales.

Phase 2: Develop the most promising technologies.

- Duration: 18 months
 - Two Technical Goals Need to be Met:
- (1) Mature the leading technologies to overcome the challenges in the focus areas; and
 - (2) Demonstrate spatiotemporal resolution goals in appropriate preclinical biological models.

Phase 3: Integrate the best technologies to result in a working prototype ready for advanced validation in humans.

- Duration: 12 months
 - One Technical Goal is Needed:
- (1) Validate the techniques to register low- and high-resolution images.

Program managers must be able to terminate underperforming areas and shift those resources to well performing ones. Regular reviews are necessary and may be as frequent as phone calls every week, short visits every month and semiannual formal reviews. Such an approach requires a small efficient bureaucracy. ARPA-H will be based on the DARPA model of an agency director, office directors and program managers. Authority and responsibility will be hierarchical with the Agency Director having final approval authority. Office managers will have authority over their program managers and programs. The program manager will have the authority to hire/fire performing teams and redirect monies within the program. To stay relevant, the Director, office directors and program managers must serve under term limits, on the order of 3-6 year tenures.

Attachment—Additional Questions for the Record

**Subcommittee on Health
Hearing on
"ARPA-H: The Next Frontier of Biomedical Research"
February 8, 2022**

Admiral Brett P. Giroir, M.D., Former Assistant Secretary for Health, U.S. Department of Health and Human Services

The Honorable Michael C. Burgess, M.D. (R-TX)

1. You have one of the strongest understandings of the DARPA program. You have worked with the program both on the private research and development side, and on the administrative side while serving as the Director of the Defense Sciences Office. What did you learn about the structure of DARPA during this time and involvement with the program, and do you believe any of these qualities should be applied to ARPA-H?

ANSWER

The structure of ARPA-H, like that of DARPA, must be one that promotes innovation, speed, agility, and boldness without fear of failure. In order to achieve this, the organization must be small (DARPA has only ~100 technical staff), flat (few layers of command and control), and unencumbered by bureaucratic processes. The program managers and leadership should not have to answer to external officials who do not understand the culture and mission of DARPA/ARPA-H. Funding for small highly innovative proposals should be provided within weeks, and the agency must be allowed to design a balanced and risk-adjusted portfolio in order to achieve national objectives. The structure must also support frequent and transparent communication to Congress, industry, academy, NGOs, and patient advocacy support groups. My last year at DARPA as an office director, I did 113 formal briefings, and about one-quarter of those were to Members of Congress or professional staff.

The Honorable Gus Bilirakis (R-FL)

1. Dr. Giroir, Operation Warp Speed proved that with the proper agency coordination, funding, and partnership with the private sector, we can accomplish an acceleration of biomedical research and development, ultimately leading to approval of treatments – and this was done all under the existing federal agency framework. Can you tell me how you believe ARPA-H could replicate this success, if at all, instead of bogging down our existing infrastructure?

ANSWER

OWS was a tremendous success, but its success was acceleration and financial de-risking of relatively standard processes based on science that was funded 8 years earlier by

DARPA. ARPA-H must be designed to innovate, perhaps radically, and then transition those innovations either to the private sector or to public-private-partnerships (like OWS) to perform the final implementation. DARPA invented the internet (ARPA-net), but DARPA did not need to implement the internet to make it successful. DARPA invented stealth, but never operationalized or weaponized the actual combat aircraft (the Air Force did that). ARPA-H will operate at a different level of innovation, far upstream in the pipeline from programs like OWS.

2. Dr. Giroir, your testimony goes at length about the key importance of program managers at DARPA, and how it could make or break ARPA-H. Can you expand on this need for regulatory flexibility, where the private sector fits into the equation, and what challenges you would foresee if we decided to add this to the existing framework of bureaucracy?

ANSWER

Program managers are the entrepreneurs in the public's interest. They will come from all sectors, including the private sector, academia, and other government agencies. The private sector (and academia) will be benefitted substantially by the high risk- high reward research and development fostered by ARPA-H, as it has been by DARPA. Far from it, ARPA-H must cut through the typical bureaucracies of the federal government in general, and NIH in particular. It is anti-bureaucracy by its nature.

3. Dr. Giroir, you mention in your testimony that it's important that ARPA-H's director should be "strategic, visionary, and able to recruit the best and brightest program managers...". How would this work if ARPA-H is under the umbrella of the NIH as proposed by the White House?

ANSWER

The ARPA-H director must report to the Secretary. For the director to report anywhere within the NIH, or be encumbered by NIH processes, would guarantee failure of the new agency.

4. Considering the NIH is limited by statute to 27 institutes and centers, how would the White House proposal ensure that ARPA-H doesn't serve as an additional layer of bureaucracy, and where would this put the work of NCATS, whose mission is to transform scientific discoveries into new treatments and cures?

ANSWER

ARPA-H, if positioned within NIH, could indeed become just another layer of stagnation and fail to achieve its stated mission. As former NCATS director Dr. Christopher Austin described, NCATS is important but has a different mission and focus; and its inability to innovate in the way DARPA has (or ARPA-H should) is itself a testament for why ARPA-H should not be organized within the NIH, nor report to anyone except the Secretary of HHS.

Attachment—Additional Questions for the Record

Subcommittee on Health
Hearing on
"ARPA-H: The Next Frontier of Biomedical Research"
February 8, 2022

Brian J. Miller, M.D., M.B.A., M.P.H., Assistant Professor of Medicine, The John Hopkins University School of Medicine

The Honorable Michael C. Burgess, M.D. (R-TX)

1. ARPA-H is looking to accomplish what many private companies are already investing in. While I don't think any of us disagree that investment in research and development to find a cure for the "uncurable" diseases is important, the investment in ARPA-H is far less than what the private industry is currently investing. What could ARPA-H do that is not, or cannot, currently be accomplished at other agencies or within the private sector?

It would be challenging for ARPA-H to accomplish that which is currently being accomplished at other agencies and in the private sector. The National Institutes of Health Extramural Grant Program invests \$31 billion annually in biomedical research, representing nearly half of the over \$70 billion in annual federal biomedical research expenditures. The life sciences investment community puts forth over \$36 billion annually into life sciences startups.

Despite convening 10 listening sessions with over 5,100 stakeholders, the White House Office of Science and Technology Policy has not published a list of specific scientific and medical research priorities for ARPA-H. Thus, it is unclear exactly what mission gap ARPA-H will be filling that other entities, public and private, are not already fulfilling or could otherwise be re-tasked (or otherwise incentivized with existing mechanisms) to address.

Regardless, the principles of ARPA-H should be deployed: an independent professional staff, time-based milestones for research outcomes, and a target of revolutionary ideas. Policymakers would be well-served by empowering existing federal research programs to better execute on these principles. If we are to use taxpayer dollars for research, we should seek the projects that are "high risk, high return."

- a. What do you believe the most efficient way to structure ARPA-H would be, and what do you believe the goals of this agency should be?

Instead of structuring ARPA-H as an independent agency (where it would incur all the structural and management costs associated thereof) or as an institute at the National Institutes of Health (and thus face similar challenges), policymakers should

consider restructuring part of pre-existing extramural grant program along the proposed aims of ARPA-H. This could either be part of each area study section funding being “partitioned” out for a more aggressive, high-risk high-return program; a repurposing of existing programs such as NCATS; or a combination of the aforementioned.

Using a DARPA-like program-manager model or FDA “professional staff reviewer” model in place of study sections could promote more rapid decision-making, increase flexibility, and allow for positive idea risk in project selection.

Such a program should invest in areas currently not being covered by other programs, focusing on high-risk, high-reward research. Accordingly, a program should not be initiated until clear medical and scientific gaps are elucidated, and policymakers ensure that there is not overlap with pre-existing public and private research efforts.

2. Our country has a long history of looking for ways to accelerate innovation. Do you agree that before committing to a fully new program, that there are reforms that can be made to other government programs intended to spur innovation, such as the Centers for Medicare and Medicaid Innovation Center?

Before funding, authorizing, and executing a new healthcare innovation program, policymakers should examine prior federal health innovation programs, characterizing success and failures. Created in 2010, the Centers for Medicare and Medicaid Innovation Center, was authorized with a \$10 billion budget over a decade with a handful of statutorily-specified models with the rest left to agency discretion. After a decade of conducting experiments in health finance, the Chief Actuary of CMS has only certified four of over fifty models for national scaling,¹ with only two – the Diabetes Prevention Program^{2,3} and components of the Pioneer ACO model – scaled nationally within the Medicare program.⁴ Market impact of the CMS Innovation Center has been limited: despite over 16.4 million beneficiaries estimated to meet eligibility criteria for the Diabetes Prevention Program,⁵ by 2019 only 200 beneficiaries had enrolled.⁶ The Pioneer ACO model exhibited similar challenges during its trial period, with

¹ Berwick DM, Gilfillan R. “Reinventing the Center for Medicare and Medicaid Innovation.” *JAMA* 325(13):1247-1248.

² *Independent experts confirm that diabetes prevention model supported by the Affordable Care Act saves money and improves health.* (2016) Retrieved from <https://wayback.archive-it.org/3926/20170127185647/https://www.hhs.gov/about/news/2016/03/23/independent-experts-confirm-diabetes-prevention-model-supported-affordable-care-act-saves-money.html>

³ Medicare Diabetes Prevention Program Expansion. Centers for Medicare & Medicaid Services (2016). Available from: <https://www.cms.gov/newsroom/fact-sheets/medicare-diabetes-prevention-program-expansion>

⁴ Berwick, DM., Gilfillan, R. (2021) Reinventing the Center for Medicaid and Medicare Innovation. *JAMA*. 2021;325(13):1247–1248. doi:10.1001/jama.2021.3203

⁵ Meyer H. (2021). Medicare Diabetes Prevention: Enrollment Short Of Projections. *Health Affairs (Project Hope)*, 40(11), 1682–1687. <https://doi.org/10.1377/hlthaff.2021.01292>

⁶ Tahir, D. (2019). Medicare diabetes prevention program helps a few hundred instead of hundreds of thousands. *Politico*. Retrieved from <https://www.politico.com/news/2019/10/22/medicare-diabetes-hhs-055006>

approximately one-third of providers remaining enrolled during the initial three-year performance period.⁷ The achieved (i.e. executed) value of scale CMS Innovation Center programs for taxpayers is a source of debate, albeit is likely less than the initial programmatic investment and even smaller when ignoring the opportunity cost of human capital deployed. Before undertaking any similar program for further funding biomedical innovation, a neutral third party such as the National Academy of Medicine (in consultation with relevant private sector stakeholders) should undertake a thorough assessment of the successes and failures of CMS so as to avoid repeating prior mistakes in another innovation policy arena.

- a. What are some suggestions you have for reforms to these programs, and could dollars saved from reforming these programs be reinvested in efforts like an ARPA-H?

Specifically, existing program funding focused on translational research could be redirected to this purpose. Promoting transparency and appropriateness of indirect costs at existing institutions participating in federal research would allow for identification of specific savings. Some institutions may need high indirect costs (e.g. maintenance of a BSL-4 laboratory), while others may not.

The Honorable Gus Bilirakis (R-FL)

1. Dr. Miller, Operation Warp Speed proved that with the proper agency coordination, funding, and partnership with the private sector, we can accomplish an acceleration of biomedical research and development, ultimately leading to approval of treatments – and this was done all under the existing federal agency framework. Can you tell me how you believe ARPA-H could replicate this success, if at all, instead of bogging down our existing infrastructure?

Existing as an independent agency or as part of the NIH, ARPA-H would struggle to replicate the effects of Operation Warp Speed. In record time with a focus on achieving a scientific and operational outcome – development and mass product of vaccines, therapeutics, and diagnostics – Operation Warp Speed promoted across government coordination and elimination of regulatory barriers all driven by a sense of urgency if not emergency. It is unlikely that a single agency would be able to replicate this success. Consumers would be better served by examining regulatory policy barriers to lower the cost and increase the speed of drug and device development, given the massive existing public and private infrastructure already spent on biomedical research.

⁷ “Evaluation of CMMI Accountable Care Organization Initiatives: Pioneer ACO 2016 Final Report.” L&M Health Policy Research 2016. Retrieved from <https://innovation.cms.gov/files/reports/pioneeraco-finalevalrpt.pdf>