

**21ST CENTURY CURES IMPLEMENTATION:
UPDATES FROM FDA AND NIH**

HEARING
BEFORE THE
SUBCOMMITTEE ON HEALTH
OF THE
COMMITTEE ON ENERGY AND
COMMERCE
HOUSE OF REPRESENTATIVES
ONE HUNDRED FIFTEENTH CONGRESS
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21ST CENTURY CURES IMPLEMENTATION: UPDATES FROM FDA AND NIH

WEDNESDAY, JULY 25, 2018

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

The subcommittee met, pursuant to call, at 9:04 a.m., in room 2123, Rayburn House Office Building, Hon. Michael Burgess, M.D. (chairman of the subcommittee) presiding.

Present: Representatives Burgess, Guthrie, Barton, Upton, Blackburn, Latta, Lance, Griffith, Bilirakis, Long, Bucshon, Brooks, Mullin, Hudson, Collins, Carter, Walden (ex officio), Green, Schakowsky, Matsui, Castor, Sarbanes, Kennedy, Cárdenas, Eshoo, DeGette, and Pallone (ex officio).

Staff Present: Daniel Butler, Legislative Clerk, Health; Jordan Davis, Senior Advisor; Adam Fromm, Director of Outreach and Coalitions; Caleb Graff, Professional Staff Member, Health; Ed Kim, Policy Coordinator, Health; Ryan Long, Deputy Staff Director; Brannon Rains, Staff Assistant; Mark Ratner, Policy Coordinator; Kristen Shatynski, Professional Staff Member, Health; Danielle Steele, Counsel, Health; Austin Stonebraker, Press Assistant; Josh Trent, Chief Health Counsel, Health; Hamlin Wade, Special Advisor, External Affairs; Waverly Gordon, Minority Health Counsel; Tiffany Guarascio, Minority Deputy Staff Director and Chief Health Advisor; Samantha Satchell, Minority Senior Policy Analyst; Andrew Souvall, Minority Director of Communications, Outreach and Member Services; Kimberlee Trzeciak, Minority Senior Health Policy Advisor; and C.J. Young, Minority Press Secretary.

OPENING STATEMENT OF HON. MICHAEL C. BURGESS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS

Mr. BURGESS. The Subcommittee on Health will now come to order. I recognize myself 5 minutes for an opening statement.

This morning, I certainly want to welcome our witnesses. We are here to conduct oversight and receive updates on the implementation on one of the most substantial legislative accomplishments in the space of biomedical innovation, the 21st Century Cures Act. Cures passed both the House and the Senate with wide bipartisan support. It was signed into law December, 2016. As with all landmark laws, I think it is critical that the Congress, especially the relevant authorizing committee, engage in oversight to ensure that the agencies are implementing the law according with legislative intent, based upon the active leadership and robust activities of

both the National Institutes of Health and the Food and Drug Administration.

I look forward to hearing from Dr. Francis Collins, Director of National Institutes of Health, and Dr. Scott Gottlieb, the Commissioner of the Food and Drug Administration, regarding progress in implementing Cures. I thank our witnesses for their willingness to testify on such an important topic.

The 21st Century Cures Act provides hope to those who need it the most, individuals and families suffering from life-altering, often life-threatening illnesses, whether it is cancer, or a rare disease, or Alzheimer's. There are conditions that are costly to Americans of all ages and their families. Sadly, we each know too well the financial and the human toll that diseases place on our friends and our communities.

One of the most impactful positions of the 21st Century Cures created the NIH Innovation Account in Treasury. This account funds projects like those related to Precision Medicine Initiative, the Brain Research Through Advancing Innovative Neurotechnologies Initiative, cancer research and regenerative medicine. The pace and breadth of biomedical research continues to accelerate, as we now have treatments to cure diseases, such as Hepatitis C, which was once unimaginable. Yet there is still much we do not know, especially regarding the neurodegenerative diseases.

21st Century Cures included a provision to establish a National Neurological Conditions Surveillance System. Prior to Cures, there was no requirement or authorization to provide surveillance of neurologic disease, but this changed, thanks to Cures. Specifically, this section of law requires the Secretary of the Department of Health and Human Services to create such a system by expanding surveillance, infrastructure, and activities, including data collection, to determine prevalence, risk factors, and diagnostic and progression markers.

Preliminary results from an ongoing Multiple Sclerosis Society study show that there are nearly 1 million Americans living with MS, more than twice the previously reported number. The surveillance system included in Cures will provide us better information so that we can further our understanding of, and eventually cure these diseases. I am especially grateful to see progress on this important policy. This began as a standalone bill introduced in the previous Congress.

Additionally, Cures advanced precision medicine, which allows physicians to offer their patients truly personalized treatment. Achieving the full potential of precision medicine will require effort to collect health data in addition to the research done by our nation's best research investigators. The law codifies the Precision Medicine Initiative, and encourages the Secretary of Health and Human Services to carry out the goals of the initiative while ensuring confidentiality of the patient's information. The All of Us Research Program is a major piece of the Precision Medicine Initiative, and has already engaged over 1 million volunteers in the United States. I think you are to be congratulated for that.

Clinical trials play a crucial and necessary role in the drug approval process. While the Food and Drug Administration's tradi-

tional clinical trial methods have proven successful, they are not always timely or applicable to new types of drugs. Cures requires the Food and Drug Administration to evaluate its trial designs and issue guidance for the purposes of “incorporating complex adaptive and other novel trial designs.”

The innovation and promising results of efforts included in Cures will provide Americans suffering from cancer and other diseases with the opportunity to undergo successful treatments, and to, in some cases, be cured.

So our thanks to Dr. Collins, Dr. Gottlieb, for giving us the updates on the implementation of this new law.

I will yield the balance of my time to the gentlelady from Tennessee, Mrs. Blackburn, for a statement.

[The prepared statement of Mr. Burgess follows:]

PREPARED STATEMENT OF HON. MICHAEL C. BURGESS

Today, we are here to conduct oversight and receive updates on implementation of one of the most substantial legislative accomplishments in the space of biomedical innovation—the 21st Century Cures Act. Cures passed both the House and the Senate with wide bipartisan support and was signed into law in December of 2016. As with all landmark laws, I think it is critical that the Congress, especially the relevant authorizing Committee, engage in oversight to ensure that the agencies are implementing the law successfully.

Based on the active leadership and robust activities of both the National Institutes of Health and the Food and Drug Administration, I look forward to hearing from Dr. Francis Collins, Director of the National Institutes of Health (NIH), and Dr. Scott Gottlieb, Commissioner of the Food and Drug Administration (FDA), regarding progress in implementing provisions of Cures. I thank both of our witnesses for their willingness to testify on such an important topic.

The 21st Century Cures Act provides hope to those who need it the most—individuals and families suffering from life-altering, often life-threatening illnesses. Whether it be cancer, a rare disease, or Alzheimer’s, there are countless conditions that are costly to Americans of all ages and their families. Sadly, we each know too well the financial and human toll that diseases place on our friends and communities.

One of the most impactful provisions in 21st Century Cures created the NIH Innovation Account in the Treasury. This account funds projects related to the Precision Medicine Initiative (PMI), the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, cancer research, and regenerative medicine. The pace and breadth of biomedical research continues to accelerate, as we now have treatments to cure diseases such as Hepatitis C, which was once unthinkable. Yet, there is still much we do not know, especially regarding neurodegenerative diseases.

21st Century Cures also included a provision to establish a National Neurological Conditions Surveillance System. Prior to Cures, there was no requirement or authorization to provide surveillance of neurological diseases. But this has changed thanks to the Cures law.

Specifically, this section of the law requires the Secretary of the Department of Health and Human Services to create such a system by expanding surveillance infrastructure and activities, including data collection to determine prevalence, risk factors, and diagnostic and progression markers. Preliminary results from an ongoing MS Society study show that there are nearly one million Americans living with MS, more than twice the previously reported number. The surveillance system included in Cures will provide us with better information so that we can further our understanding of, and eventually cure, these diseases. I am especially grateful to see progress on this important policy, as this part of the law began as a standalone bill that I introduced last Congress.

Additionally, Cures advanced precision medicine, which allows physicians to offer their patients truly personalized treatment. Achieving the full potential of precision medicine will require immense efforts to collect health care data in addition to research done by our nation’s best research investigators. This law codifies the Precision Medicine Initiative and encourages the Secretary of HHS to carry out the goals of the initiative while ensuring confidentiality of patients’ information. The All of

Us Research Program is a major piece of the PMI and has already engaged over 1 million volunteers in the U.S.

Clinical trials play a crucial, and necessary, role in the drug approval process. While FDA's traditional clinical trial methods have proven successful, they are not always timely or applicable to new types of drugs. Cures requires the FDA to evaluate its trial designs and issue guidance for the purpose of "incorporating complex adaptive and other novel trial designs."

The innovation and promising results of efforts included in Cures will certainly provide Americans suffering from cancer and other diseases with the opportunity to undergo successful treatments, and in some cases, to be cured.

Thank you to Drs. Collins and Gottlieb for giving us updates on the implementation of this important law. I look forward to hearing your testimony.

I yield the balance of my time to the gentlelady from Tennessee, Ms. Blackburn, for a statement.

Mrs. BLACKBURN. Thank you, Mr. Chairman.

And Dr. Collins and Dr. Gottlieb, we are delighted that you are here. Two things that I am going to want to discuss with you all. Dr. Collins, the All of Us Research project, and making certain that we anonymize, and that we protect the data that is in that program, and that the privacy of the patients with data is respected as we move forward with this.

And, Dr. Gottlieb, following up on the SOFTWARE Act and making certain that the implementation is going well. And we welcome you both. We look forward to the hearing.

I yield back.

Mr. BURGESS. The chair thanks the gentlelady. The chair yields back.

The chair now recognizes the gentleman from Texas, the ranking member of the subcommittee, Mr. Green, 5 minutes for an opening statement, please.

**OPENING STATEMENT OF HON. GENE GREEN, A
REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS**

Mr. GREEN. Mr. Chairman, thank you for holding today's hearing on the Implementation of the 21st Century Cures Act. I want to thank all our witnesses for being here today, especially Dr. Collins from NIH and Dr. Gottlieb from FDA—you are pretty regulars at that table—for being here.

This December will mark the 2-year anniversary of the 21st Century Cures Act being signed into law by President Obama in his last public signing ceremony. The promise of the 21st Century Cures is to advance the discovery and development of new treatments, cures, through increased research and improved drug approval process.

This important law dedicated \$6.3 billion in new investments to support medical research initiatives, like the Beau Biden Cancer Moonshot, the BRAIN Initiative, the Precision Medicine Initiative within the National Institutes of Health. It also provides money to the Food and Drug Administration to advance the agency's mission and implement the policies in the underlying bill.

I hope, our committee and Congress, that these investments are being put toward finding a cure for many of our nation's greatest medical priorities and ensuring the infrastructure is in place so the new therapies are accessible to all Americans.

The NIH was provided \$4.8 billion in new funding and advanced cutting-edge research initiatives. The FDA was provided \$500 mil-

lion over 10 years to improve the agency's medical product review process and expedite patient access to drugs and devices without compromising standards of safety and effectiveness.

In addition to this much-needed funding, there are many provisions in this package worthy of support, from facilitating the development of new antibiotics to fight against superbugs through advancing the use of modern clinical trial designs to investing in the next generation of medical researchers. While some of the provisions are technical in nature, the real-world impact could not be abstract.

Patients and families deserve to have their elected officials respond to their needs. The 21st Century Cures was written to do just that. This morning is an opportunity to hear from the heads of the FDA and NIH on implementation of the many provisions of this law, from patient-focused drug development, medical device innovation, and improving scientific expertise and hiring capacity. Many members of our committee were instrumental in getting Cures developed and signed into law. Most notably, Representative Diana DeGette and Representative Fred Upton.

The 21st Century Cures Act demonstrates what we can accomplish when we work across the aisle. I look forward to hearing from our witnesses about the oncoming implementation of 21st Century Cures.

Mr. Chairman, I yield the remainder of my time to my colleague, Congressman Diana DeGette.

[The prepared statement of Mr. Green follows:]

PREPARED STATEMENT OF HON. GENE GREEN

Mr. Chairman, thank you for holding today's hearing on the implementation of the 21st Century Cures Act.

I thank Dr. Collins and Dr. Gottlieb for being here this morning.

This December will mark the 2 year anniversary of the 21st Century Cures Act being signed into law by President Obama in his last public signing ceremony.

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velopment, medical device innovation, and improving scientific expertise and hiring capacity.

Many Members of our committee were instrumental in getting Cures developed and signed into law, most notably Representatives Diana DeGette and Fred Upton.

The 21st Century Cures Act demonstrates what we can accomplish when we work across the aisle.

I look forward to hearing from our witnesses about the ongoing implementation of the 21st Century Cures Act.

Thank you Mr. Chairman, and I yield the remainder of my time to Congresswoman DeGette.

Ms. DEGETTE. Thank you so much, Mr. Chairman, or Mr. Ranking Member, for yielding.

And I just want to add my thanks to everybody here, in particular, Dr. Collins and Dr. Gottlieb, and all of their staff who helped us develop this bill, most especially my compadre, Fred Upton, who is sitting over there, who really worked with us every day.

But this really was a work product of this entire committee, and it shows the greatness of the Energy and Commerce Committee and what we can do when we decide to work together to tackle a serious problem.

Mr. Chairman, I also want to thank you for having this series of hearings. It is about a year and a half since the bill has been signed, and it is almost exactly 2 years since we originally passed it through this committee. We need to make sure that everything we intended to do in Cures is happening, and if the agencies need modifications or changes or additional resources that we give that all due consideration. And the only way we can do that is to have hearings like this.

I do want to say I have been concerned lately reading some media accounts that say that some of the Cures money may be reprogrammed for other purposes, including for the ORR issues of the kids at the border. We should be able to find the money to do that without taking money away from important biomedical research and drug and device approval at the FDA.

So I hope that is not the case; and if it is, I hope this committee acts swiftly and in a bipartisan way to make sure that the intended moneys that we authorized in this committee remain, because we still have so many bridges to cross and we are going to need every penny that we authorized.

With that, thank you very much, Mr. Green, for yielding, and I yield back.

Mr. GREEN. Mr. Chairman, I yield back.

Mr. BURGESS. The chair thanks the gentleman. The gentleman yields back. Pending the arrival of the chairman of the full committee, the chair now recognizes the ranking member of the full committee, Mr. Pallone of New Jersey, 5 minutes for an opening statement, please.

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

Mr. PALLONE. Thank you, Mr. Chairman. I want to thank Dr. Collins, Dr. Gottlieb, Dr. Sharpless, and Dr. Devaney for joining us to discuss the ongoing work at NIH and FDA to implement the

21st Century Cures Act. And, of course, I also want to thank our colleagues Diana DeGette and Fred Upton, without which the Cures Act would never have become law.

The Cures Act tasks both of your agencies with implementing critical provisions aimed at improving the discovery and development of new treatments and cures. At NIH, the law provided significant funding for the Beau Biden Cancer Moonshot Initiative, the All of Us Research Program, and the BRAIN Initiative; and at FDA, the law included provisions to improve the medical product review process, as well as new authorities and funding to ensure the agency has the resources to recruit the best talent.

At our hearing on this topic last November, you both provided promising updates, and I look forward to your continued work. As I said before, it is important to hold oversight hearings like these that allow us to learn directly from the administration how policies are being implemented.

While I am pleased that the subcommittee has decided to conduct continued oversight of the Cures Act, there are several topics within the subcommittee's jurisdiction that also deserve hearings and oversight. For example, I have asked the majority to schedule hearings on a number of issues that are priorities for Democratic members of the committee. I have asked for hearings on maternal mortality, health disparities, gun violence, the Indian Health Service, cosmetics reform, the Office of Refugee Resettlement, drug pricing, abuse of the REMS program, and marketplace stabilization.

These are all different issues within the subcommittee's jurisdiction, and we may have different opinions on many of them. That is exactly why we should at least have a hearing. And these are critical issues that this committee should be discussing in an effort to find potential solutions.

So I hope in the coming weeks, after the August recess, that the chairman will respond and select a few of these issues to hold hearings on in the short time we have left for this Congress.

And unless someone else wants my time, I yield back, Mr. Chairman.

[The prepared statement of Mr. Pallone follows:]

PREPARED STATEMENT OF HON. FRANK PALLONE, JR.

I want to thank Dr. Collins, Dr. Gottlieb, Dr. Sharpless, and Dr. Devaney for all joining us to discuss the ongoing work at NIH and FDA to implement the 21st Century Cures Act.

The Cures Act tasked both of your agencies with implementing critical provisions aimed at improving the discovery and development of new treatments and cures. At NIH the law provided significant funding for the Beau Biden Cancer Moonshot Initiative, the All of Us Research Program, and the BRAIN Initiative. And at FDA, the law included provisions to improve the medical product review process, as well as new authorities and funding to ensure the agency has the resources to recruit the best talent.

At our hearing on this topic last November you both provided promising updates and I look forward to your continued work. As I've said before, it's important to hold oversight hearings like these that allow us to learn directly from the Administration how policies are being implemented.

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parities, gun violence, the Indian Health Service, cosmetics reform, the Office of Refugee Resettlement, drug pricing, abuse of the REMS program, and marketplace stabilization.

These are all different issues within this Subcommittee's jurisdiction, and we may have different opinions on many of them, but that's exactly why we should at least have a hearing. These are critical issues that this Committee should be discussing in an effort to find potential solutions.

I hope that in the coming weeks the Chairman will respond to my requests and select a few of these issues to hold hearings on in the short time we have left this Congress.

I yield back.

Mr. BURGESS. The chair thanks the gentleman. The gentleman yields back. The chair will hold the time for the opening statement of the chairman of the full committee, pending his arrival.

We thank our witnesses for being here today and taking time to testify before the subcommittee. I am going to give our witnesses an opportunity to give an opening statement. That will be followed by questions from members.

Today, we are going to hear from the Honorable Francis Collins, the Director of the National Institutes of Health; and the Honorable Scott Gottlieb, Commissioner of the Food and Drug Administration. And Dr. Collins, it is my understanding you have brought a supporting cast of Dr. Norman Sharpless, the 15th Director of the National Cancer Institute; and Dr. Stephanie Devaney, who is the Deputy Director of the All of Us Research Program. I don't know if it is the intention for all of you to give an opening statement, but we will start with you then, Dr. Collins, and you are recognized for 5 minutes for an opening statement, please.

STATEMENTS OF HON. FRANCIS COLLINS, DIRECTOR, NATIONAL INSTITUTES OF HEALTH, ACCOMPANIED BY DR. STEPHANIE DEVANEY, DEPUTY DIRECTOR, ALL OF US RESEARCH PROGRAM, DR. NORMAN SHARPLESS, DIRECTOR, NATIONAL CANCER INSTITUTE; AND HON. SCOTT GOTTLIEB, COMMISSIONER, FOOD AND DRUG ADMINISTRATION.

STATEMENT OF DR. FRANCIS COLLINS

Dr. COLLINS. Thank you and good morning, Chairman Burgess, Ranking Member Green, and other distinguished committee members. It is a great honor to appear before you again today, along with my colleague, FDA Commissioner Dr. Scott Gottlieb, to give you a progress report on our implementation of the 21st Century Cures Act. Also joining me, as you have just introduced, the head of the Cancer Institute, Ned Sharpless; and Deputy Director of the All of Us Program, Dr. Stephanie Devaney.

I can't emphasize enough for this subcommittee how much we appreciate your bipartisan leadership in passing this Act—51 to nothing, as I recall, out of Energy and Commerce—which aims to speed the translation of scientific discoveries into life-saving treatments and cures. In the written statement I have submitted, I have outlined a comprehensive report on how NIH is working swiftly to implement the Act's provisions one by one.

That most especially includes multiyear support for four specific areas of scientific opportunity supported by the Act's Innovation Fund. Today, I would like to highlight two of these: The Cancer

Moonshot, and the bold new Precision Medicine Initiative, called All of Us.

The Cancer Moonshot is aggressively pursuing a very ambitious goal to accelerate advances in cancer prevention, diagnosis, treatment and care. Such advances include immunotherapy, in which a person's own immune system is taught to recognize and attack cancer cells. After years of research supported by NIH, immunotherapy is leading to dramatic cures of some cancers, like leukemia, lymphoma, and melanoma. But some other cancers, particularly solid tumors, like colon, pancreas, breast and prostate, have proven much less responsive.

Thank you. The slides are now up there.

I am thrilled to tell you that some of those barriers seem ready to come down. Just last month, a team led by NIH's Dr. Steven Rosenberg announced a novel modification of an immunotherapy approach that led to a complete regression, most likely a cure, of widely metastatic breast cancer in a woman with previously, universally fatal form of the disease. As always, I have to counsel patients this success story for solid tumors, like breast cancer, involves very few cases right now, and must be replicated in further studies; but without doubt, this woman's life-saving experience represents hope for millions more.

As exciting as potential cures like this can be, in authorizing and funding the Cancer Moonshot, you wisely tasked NIH with advancing not just cancer therapies, but also cancer care. Let me tell you about an NIH-funded trial that beautifully illustrates the progress we are making in this area. Each year, as many as 135,000 American women who have undergone surgery for the most common form of early stage breast cancer, face a very difficult decision, whether or not to also undergo chemotherapy to improve their odds. Now, thanks to a large NIH-funded clinical trial called TAILORx, we finally have some answers, and they are good answers. It turns out that about 70 percent of such women actually do not benefit from chemotherapy, and a genomic test of tumor tissue can identify them quite reliably.

Clearly, it is ideal to spare women from the potential toxic side effects of chemotherapy, if that is possible, and still have a good outcome. On top of that, and this will probably warm your heart, because it certainly does mine, this move, basically making it not necessary to go through chemotherapy for many of those women, will produce a significant cost savings for our healthcare system, maybe up to \$1 billion a year.

Figuring out what health approaches work best for each individual and why brings me to the goal of another important investment of the Cures Innovation Fund, and that is, the Precision Medicine Initiative. The centerpiece of this initiative, the All of Us Research Program, will enroll 1 million or more people, and we are off to a very strong start. On May 6, just 2 months ago, the day we launched national enrollment in seven sites across the Nation, we reached more than 10,000 people just that day at community events, and almost four times that number online.

As of this week, over 86,000 volunteers have signed up to contribute their health data in many ways over many years. Some are enrolled through health provider organizations, ten of them that

are part of our enterprise, and that includes community health centers and the Department of Veterans Affairs. Others enroll as direct volunteers, who sign up over the internet. Altogether, I am happy to tell you that almost half are from historically underrepresented racial and ethnic groups, which is one of our goals, so that we can utilize this to look at health disparities.

Right now, anyone who is 18 and older, including Members of Congress—note the URL if you are interested in learning more about how to sign up—you can join. Next year, we will begin enrolling children. We decided to first start with adults, but next year, children will be added in. And in 2019, we plan to open a secure portal to give researchers access to All of Us data in a deidentified format with exceptional security.

With every new person enrolled, every biological sample preserved, every electronic health record collected, every survey filled out, this data will hold more and more promise for advancing human health. And with every new scientist mining this data in search of answers to the important biomedical questions, the more that promise will be realized. This is groundbreaking.

This exciting progress, along with many other advances in biomedical research, is being made possible because of the vision of you and your colleagues. So thank you for your investment in the 21st Century Cures Act, as well as your ongoing support of NIH. We could not do this without you.

My colleagues and I really look forward to your questions. Thank you.

[The prepared statement of Dr. Collins follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Hearing on "21st Century Cures Implementation: Updates from
FDA and NIH"

Witness appearing before the
House Committee on Energy and Commerce Subcommittee on Health

Francis S. Collins, M.D., Ph.D.
Director, National Institutes of Health

Accompanied by
Norman E. "Ned" Sharpless, M.D.
Director, National Cancer Institute
and
Stephanie Devaney, Ph.D.
Deputy Director, *All of Us* Research Program

July 25, 2018

Chairman Burgess, Ranking Member Green, Distinguished Members of this Subcommittee, thank you for hosting this important hearing.

The 21st Century Cures Act (Cures Act) touches on so many important issues. From providing support for four cutting edge research priorities, to enhancing privacy protections to inclusion of various communities in research trials, to reducing administrative burden to expanded prize authority, we at NIH appreciate your leadership and dedication in enacting new authorities to speed the pace of research and improve how science is conducted to transform the way we translate discovery into therapies.

In my testimony, I will update you on how NIH is implementing some of the key provisions of the Cures Act and how it is benefiting the biomedical research community and, most importantly, patients and the general public.

Big Data: The Promise of Data Sharing Balanced With the Need for Privacy

As in most fields, computing power is changing the way research is done. The promise of big data cannot be overstated for finding patterns of disease and health and targeting therapeutics to sub-populations. The Congress, in the Cures Act, wisely recognized both the potential and the risks inherent in sharing data sets and NIH has moved quickly to get the appropriate protections in place.

First, on September 7, 2017 NIH issued a Guide Notice to our research community implementing the significant enhancements this Committee made to the Certificates of Confidentiality, making them both automatic and compulsory. To implement this change while minimizing the burden to our researchers, we streamlined the issuance of Certificates into the

terms and conditions of every research award we make involving human subjects.¹ Since October 1, 2017 every NIH award has this added layer of protection for research participants.

Second, on September 17, 2017 guidance on the FOIA exemption for genomic information was disseminated to all NIH FOIA officers.

Only now that the new Cures Act privacy protections are in place, are we moving forward on the exciting new authority to require data sharing. This will be a sea change in biomedical research so we must be deliberate about how to measure the usefulness of data sets, where shared data should be stored, how patient protections are insured, how interoperability is achieved, and what tools researchers most need in the shared environment. On November 6, 2017 NIH made 12 awards in a Data Commons Pilot to answer just these kind of questions. We selected three prominent NIH datasets researchers can use to test their processes. The biomedical research community will be watching this pilot program very closely.

Relatedly, this spring NIH published the Strategic Plan for Data Science,² a multi-year plan to make big data sustainable, interoperable, accessible, and usable. A key component of the Strategic Plan for Data Science is NIH's effort to hire a Chief Data Strategist. The Chief Data Strategist will report directly to the NIH Director and will lead the coordination of data science activities across NIH. We have seen exponential growth in biological sciences data production and look forward to meeting the challenges and leveraging the opportunities provided by data science in the months and years ahead. Through implementation of the Strategic Plan for Data Science, NIH will maximize the potential of existing data, enable new directions for research, increase accuracy, and support precision methods for healthcare.

¹ <https://humansubjects.nih.gov/coc/index>.

² https://datascience.nih.gov/sites/default/files/NIH_Strategic_Plan_for_Data_Science_Final_508.pdf.

Inclusion

We've made tremendous progress in managing diseases through the development of new drugs and devices over the years that were tested in clinical trials. But trials haven't always included the full spectrum of humanity, and this limits the applicability of study results. It also limits our ability to target therapies and address disparities. Congress helped NIH address this issue through the Cures Act in three focus areas: inclusion of children and seniors; inclusion of pregnant and lactating women; and continuing our focus on women, and racial and ethnic minorities.

On June 1-2, 2017 as required by the Cures Act, NIH held a workshop on inclusion across the lifespan. It might seem easy to include all age ranges but both children and older adults require special considerations. At the workshop, investigators with expertise in conducting clinical studies with pediatric and older populations, ethics experts, and other stakeholders had a robust discussion about barriers and facilitators to the inclusion of volunteers of all ages in research. The findings and recommendations were presented at my Advisory Committee meeting on December 14-15, 2017, and on December 19, 2017 we announced that we were revising the NIH Policy and Guidelines on the Inclusion of Children to apply to individuals across the lifespan.³ The revisions broaden the policy to address inclusion of research participants of all ages and will apply beginning in January 2019 to all NIH-supported research involving human subjects.

The Cures Act also asks NIH to continue making progress on the inclusion of women and ethnic and racial minority populations in research. This has been a partnership of the Congress and NIH for many years – the Congress authorized both the NIH Office of Research on

³ <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-116.html>.

Women's Health and what is now the National Institute on Minority Health and Health Disparities in 1993. With the help of the Congress and the Cures Act, we continue to improve our monitoring and implementation of inclusion in these important areas. We are now collecting inclusion data on a study-by-study basis. In the coming year NIH will report, for the first time, inclusion data from studies on a disease and condition basis.

Finally, the Cures Act created a Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) to advise the Secretary of Health and Human Services regarding gaps in knowledge and research on safe and effective therapies for pregnant women and lactating women.⁴ This area of research is vital, but it is absolutely critical that we carefully consider the risks of exposures in this potentially vulnerable time of life. NIH established PRGLAC on March 13, 2017 bringing together federal and non-federal experts, including the Food and Drug Administration, representatives from relevant medical societies, non-profit organizations, and industry, to discuss these important issues.

PRGLAC has already held four public meetings – the first on August 21-22, 2017 to determine the scope of current Federal research and regulatory activities on safe and effective therapies for pregnant and lactating women, the second on November 6-7, 2017 to understand the ethical issues surrounding research to develop therapies for pregnant and lactating women, the third on February 26-27, 2018 to discuss communication strategies for health care providers and the public about the use of therapies for pregnant and lactating women, and the fourth on May 14-15, 2018 to discuss recommendations to address the gaps in knowledge, ethical issues, and communication strategies for therapies used by pregnant and lactating women. In addition, NIH issued a Request for Information to further inform the task force's deliberations.

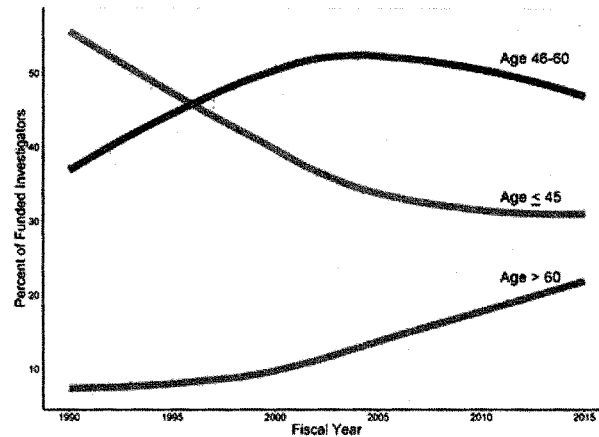
⁴ <https://www.nichd.nih.gov/about/advisory/PRGLAC/Pages/index.aspx>.

Based on the outcome of the Task Force meetings, a report with the final recommendations has been developed and will be sent to the HHS Secretary and Congress by September 2018. NIH is grateful to the Congress for recognizing the need for careful consideration in this area of research and looks forward to addressing any recommendations made by the Task Force, as determined by the Secretary.

Strengthening Biomedical Workforce

NIH and its stakeholder community have for many years been concerned about the long-term stability of the biomedical research enterprise. As a consequence of NIH's loss of more than 20 percent of its purchasing power from 2003 to 2015, researchers were forced to vie for limited resources, leading to a hypercompetitive environment. With success rates below 20 percent, many highly meritorious applications were going unfunded. This too often resulted in misaligned incentives and unintended consequences for talented researchers at all career stages who were trying to succeed and stay in science. This kind of environment can be particularly challenging for many new- and mid-career investigators.

Over the last several years, NIH has taken numerous steps to balance, strengthen, and stabilize the biomedical research workforce, but these measures have only taken us so far. While by 2015 the percentage of NIH awards that support early-career investigators went from declining to flat, those gains were offset by a decline in the percentage of NIH awards that supported mid-career investigators.



As a direct result of the Cures Act, in June 2017 NIH launched the Next Generation Researchers Initiative⁵ aimed at strengthening the biomedical workforce with a focus on early career investigators or investigators who are at an early stage in their career. NIH intends to take a multi-pronged approach, which we outlined in an article published on November 7, 2017,⁶ to increase the number of NIH-funded early-stage investigators and to stabilize the career trajectory of scientists at all stages.

NIH is developing evidence-based, data-driven strategies to assure that NIH investments are directed in ways that maximize scientific output. We are being aided in these efforts by an expert Working Group of the Advisory Committee to the Director, who will present recommendations in December 2018. But several important steps are already being taken: Institutes and Centers are placing greater emphasis on current NIH funding programs to identify, grow, and retain new- and early-career investigators across these critical career stages. The NIH

⁵ <https://grants.nih.gov/ngri.htm>.

⁶Michael Lauer, Lawrence Tabak, and Francis Collins, "Opinion: The Next Generation Researchers Initiative at NIH," *PNAS*, 114 (2017): 11801-11803.

Office of the Director is tracking progress across ICs in order to assess if these strategies are working. I am personally committed to this issue and thank the Committee for their support of early-career investigators.

System Innovation: Reducing Administrative Burden and Increasing Efficiency

The Cures Act provided NIH with new authorities to improve efficiencies and speed up the discovery process.

The Cures Act included provisions to improve ClinicalTrials.gov. ClinicalTrials.gov is a widely utilized database of privately and publicly funded clinical studies conducted around the world that plays a crucial role in helping to ensure the transparency and accountability to the public of researchers and their sponsors. In addition, this resource is used by researchers to stay up-to-date on developments in their field, find collaborators, and identify unmet needs. It is also used by patients and families to search for potential studies to enroll in or learn about new treatments that are being tested. NIH strives to make this resource as user friendly as possible so it can benefit researchers, patients, and their families, and the Cures Act is helping in several ways.

First, the Cures Act made technical fixes to the legislation establishing ClinicalTrials.gov that ensure NIH is able to capture more clinical trials in the system and improve our oversight and transparency. Second, it required NIH to consult with relevant Federal agencies and other stakeholders to receive recommendations to enhance ClinicalTrials.gov's usability, functionality, and search capability. In February 2017 the National Library of Medicine (NLM), along with 18F, a digital services consultancy within the General Services Administration, began conducting user research on ClinicalTrials.gov with a range of stakeholders. As a result of this

work, NIH rolled out a first in a series of changes to ClinicalTrials.gov on June 19, 2017. On September 25, 2017 and December 18, 2017 NLM released updates as the next phase in its ongoing effort to enhance the functionality of the database. In 2018 NLM added features for finding studies listed containing full protocols and other study documents and enhanced the information displayed about expanded access programs. In response to the Cures Act, NLM will work continuously to make it easier for users to find and participate in clinical trials.

In an effort to improve efficiency, the Cures Act provided a new EUREKA prize authority and allowed NIH to use Other Transactions Authority (OTA) in two areas that need extra flexibility and collaboration: the Common Fund and the *All of Us* Research program, part of the NIH Precision Medicine Initiative.

NIH, through the National Institute on Aging (NIA) began implementing the EUREKA prize authority in November 2017 through a request⁷ for public input on (1) the feasibility of three potential prize competitions focused on Alzheimer's disease (AD) and related dementias (ADRD): Validating predictors of AD progression; PET radiotracer to measure in vivo synaptic integrity; and low cost innovation of improving systems of care for AD/ADRD patients and caregivers; and (2) any other suggestions on AD/ADRD research goals to connect to a prize. Comments were due on December 31, 2017. The NIA considered the comments gathered and decided to move forward with a prize competition focused on innovations that have the potential to improve care for people living with AD/ADRD through the creation of a widely accessible and innovative technology tool(s) that addresses unmet needs in care coordination and/or care navigation through the health system. On June 11, 2018 the NIA launched a public comment platform⁸ to engage a broad audience in further discussion to optimize planning efforts for their

⁷ <https://grants.nih.gov/grants/guide/notice-files/NOT-AG-17-018.html>.

⁸ <https://nia-research.ideascale.com/a/ideas/recent/campaign-filter/byids/campaigns/23294/stage/unspecified>.

EUREKA prize competition. The purpose of soliciting additional public comments was to seek feedback on NIA's prize topic specifically as it related to (1) the possibility that this prize activity duplicates other ongoing activities in any relevant sector (e.g., academia, business), (2) the attractiveness of this question to a broad audience of possible solvers, (3) the length of time solvers would need to develop a prize submission, and (4) metrics that judges might use to identify a winner. Comments were due on July 1, 2018. The NIA is incorporating relevant input received into a final prize announcement for Challenge.gov, planned for release prior to September 31, 2018.

NIH also formed the EUREKA Prize Coordination Committee to review future proposals for future EUREKA prize competitions and funded the National Academy of Sciences (NAS) to study Innovation Prizes and Federal R&D with specific emphasis on strategies to determine which "EUREKA" prize topics are consistent with congressional intent. The NAS study will also consider the strengths and weaknesses of various measures of health outcomes and effects on government expenditures. The NAS intends to hold a workshop in 2018.

OTA is integral to our exploration of how best to structure data sharing, known as the Data Commons Pilot Phase,⁹ which was announced on November 6, 2017. The goal of the NIH Data Commons is to accelerate new biomedical discoveries by providing a cloud-based platform where investigators can store, share, access, and compute on digital objects (data, software, etc.) generated from biomedical research and perform novel scientific research including hypothesis generation, discovery, and validation. The use of OTA awards has allowed flexibility for the awardees to work together to design innovation solutions that meet the computational and scientific needs of the Pilot.

⁹ <https://commonfund.nih.gov/bd2k/commons/awardees>

The *All of Us* Research Program (described below) aims to enroll one million individuals in a decades-long research project. That ambitious goal requires flexibility, complex and dynamic interactions, and ways to engage non-traditional NIH awardees to advance the mission. For example, *All of Us* has used OTA to make awards to the Healthcare Provider Organizations to help build the research protocols, test enrollment procedures, and collect essential health data and biological specimens.

The Cures Act also recognizes that two of the cornerstones of scientific advancement are rigor in designing and performing scientific research and the ability to reproduce biomedical research findings. In recent years, the scientific community has become aware of the need to improve rigor and reproducibility. In 2014, NIH worked with scientific publishers to develop a set of principles and goals that 79 publishers have now endorsed. As the Cures Act requires, my Advisory Committee has convened a Working Group on Rigor and Reproducibility and they are reviewing the experience of the last few years, leading to the development of recommendations for a formal policy. I look forward to updating you as this effort takes shape.

NIH Innovation Fund

Last, but certainly not least, the Cures Act provided multi-year funding through the NIH Innovation Fund for four highly innovative scientific research initiatives: the Precision Medicine Initiative (PMI), the Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative, the Cancer Moonshot, and the Regenerative Medicine Innovation Project. As required by the Cures Act, on March 28, 2017 I solicited recommendations from my Advisory Committee on how to allocate the funds. We had a robust conversation about each of the initiatives and the Advisory Committee members provided critical advice on how to move

forward. As a result of that discussion, and conversations with my NIH colleagues, we drafted the NIH Innovation Fund Work Plan,¹⁰ which was submitted to Congress in September 2017 outlining how the agency will use the NIH Innovation Funds for each of these four initiatives. I would like to tell you a bit about each of these initiatives and how the NIH Innovation Funds are helping to move each initiative forward.

The Precision Medicine Initiative

Precision medicine is a revolutionary approach for disease prevention and treatment that takes into account individual differences in lifestyle, environment, and biology. While some applications of precision medicine have found their way into practice over the years, this individualized approach is simply not available for most diseases. The *All of Us* Research Program, a key element of PMI, is building a national resource—one of the world's largest, most diverse biomedical data sets in history—to accelerate health research and medical breakthroughs, enabling individualized prevention, treatment, and care. *All of Us* will enroll one million or more U.S. volunteers from all life stages, health statuses, races/ethnicities, and geographic regions to reflect the country's diverse places and people to contribute their health data over many years to improve health outcomes, fuel the development of new treatments for disease, and catalyze a new era of evidence-based and more precise preventive care and medical treatment.

Across the nation, NIH has engaged 10 large health provider organizations, six community health centers, and the Veterans Health Administration to be our partners in this ambitious study. The program has funded over 30 community partner organizations to motivate

¹⁰ <https://www.nih.gov/sites/default/files/research-training/initiatives/nih-cures-innovation-plan.pdf>

diverse communities to join and remain in the program, with a focus on those traditionally underrepresented in biomedical research.

We began a robust, year-long beta phase in May 2017, during which each of our partners were able to test their systems and processes to ensure a good experience for participants. I am excited to tell you that *All of Us* launched nationally on May 6, 2018 with events across the country to mark the program's open enrollment. As of July 16, 2018, 85,369 individuals have started the enrollment process, and 42,315 have completed all the steps in the protocol. Of those, I'm thrilled to tell you that 70-75% are from communities who have been historically underrepresented in biomedical research and almost 50% are specifically from racial/ethnic groups who have not been included in research.

Following the national launch, we continue to improve and adjust the program based on participant feedback and emerging scientific opportunities and technological advances. We also are currently building the All of Us data resource, which is designed to be used by a broad range of researchers to study complex risk factors, support ancillary studies and clinical trials, and link to other large data sets. The Cures Act Innovation Funds will be critical to ensuring the success of *All of Us* and the promise of personalized medicine.

The BRAIN® Initiative

The BRAIN Initiative is revolutionizing our understanding of the human brain, the most complex structure in the known universe. Launched in 2013, this large-scale effort is pushing the boundaries of neuroscience research and equipping scientists with insights necessary for treating a wide variety of brain disorders. By accelerating the development and application of innovative technologies, researchers are producing a revolutionary new dynamic picture of the

brain that, for the first time, shows how individual cells and complex neural circuits interact in both time and space. Long desired by researchers seeking new ways to treat, cure, and even prevent brain disorders, this picture is filling major gaps in our current knowledge and providing unprecedented opportunities for exploring exactly how the brain enables the human body to record, process, utilize, store, and retrieve vast quantities of information, all at the speed of thought.

NIH leveraged the Cures Act's FY 2017 Innovation Funds, in addition to our annual appropriation, to launch 110 exciting new research projects¹¹ and in FY 2018 NIH expects to fund approximately 150 new BRAIN Initiative projects. Cures funds will support critical areas including data infrastructure and sharing, the BRAIN Initiative Cell Census Network (which is developing an atlas of brain cell types), the Team Research Brain Circuits Program, and human brain studies. In human studies, the BRAIN Initiative is advancing brain imaging and non-invasive brain stimulation, and public private partnerships are investigating self-adjusting implanted brain stimulation therapies that are already showing promise. Ultimately, this will lead to an increased understanding of brain health, and a means of preventing brain disorders such as Alzheimer's disease, Parkinson's, schizophrenia, autism, drug addiction, and traumatic brain injury.

The Cancer MoonshotSM

The Cancer Moonshot,¹² funded in the Cures Act, has an ambitious goal: to dramatically speed advances in cancer prevention, diagnosis, treatment, and care. To identify the most promising and innovative strategies, the National Cancer Institute (NCI) solicited direct input from the

¹¹ <https://www.braininitiative.nih.gov/funding/fundedAwards.htm>.

¹² <https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative>.

public and convened a Blue Ribbon Panel (BRP) of the nation's top cancer researchers, oncologists, patient advocates, and private-sector leaders. In September 2016, the BRP presented its report outlining ten ambitious and achievable recommendations to the NCI's National Cancer Advisory Board. These recommendations have shaped the scientific blueprint of the Cancer Moonshot representing areas of research that are poised to accelerate our understanding of cancer and bring benefit to patients. Overall, the recommendations create a vision for future cancer research and treatment in which:

- Researchers can identify possible targets for the development of new cancer treatments and preventive interventions, including immunotherapy and immunoprevention, and learn more about how to avoid or overcome cancer drug resistance in patients;
- Diverse groups of patients contribute information about their cancer, obtain a genomic profile, learn what treatments might work best given their profile, and identify clinical trials that may be appropriate for them;
- Infrastructures are established so that health care providers and researchers can share, access, and analyze information that improves the understanding of how tumors evolve, better predicts treatment outcomes, and helps control patient symptoms and side effects.

Some of these goals are scientific in nature, and some are systemic. If we are to speed advances, we cannot simply do more of the same. We must transform the way we conduct research, the way we share results, and the way we get discoveries into patient care. In FY 2017 NIH made 142 Cancer Moonshot awards, and in FY 2018 NIH issued 17 Cancer Moonshot Funding Opportunity Announcements, including exciting opportunities in immuno-oncology for both adult and pediatric populations, and specific efforts to tackle drivers of childhood cancer.

In FY18, Innovation funds will be used to support the development of both adult and pediatric immunotherapy networks to accelerate the discovery of new immune targets and evaluate novel immune-based therapies for adults, and to identify and advance research opportunities for translating immunotherapy concepts for children and adolescents with cancer. In addition to these collaborative team science efforts, NCI is also supporting the development of a consortium to advance our understanding of the biology and mechanisms of action of fusion oncoproteins in pediatric cancers, and to apply this knowledge toward developing targeted therapeutic approaches. Increased attention to this important but understudied field can help overcome existing barriers to progress and pave the way for novel therapeutic approaches with increased efficacy and fewer side effects than current options.

With the support of the Congress, the Cancer Moonshot will transform the way cancer research is conducted and ensure that substantial progress is made for patients and their families.

The Regenerative Medicine Innovation Project

Regenerative medicine is an emerging area of science that holds great promise for treating and possibly even curing a variety of injuries and diseases. Regenerative medicine includes using stem cells and other technologies, such as engineered biomaterials and gene editing — to repair or replace damaged cells, tissues, or organs. Stem cell-based approaches are under development in labs around the world, and some have already moved into clinical trials. Such progress notwithstanding, much work remains to be done toward the development of safe and effective regenerative medicine interventions to realize the full potential of this field.

As a result of the Cures Act, NIH launched the Regenerative Medicine Innovation Project (RMIP) to support clinical research using adult stem cells while promoting the highest standards

for carrying out scientific research and protecting patient safety. The \$2 million Cures provided for this initiative in FY 2017 were amplified through matching funds and NIH Institute contributions to support research totaling \$5.4 million. NIH has worked in close collaboration with the FDA to implement the RMIP. In September, NIH made eight clinical research awards¹³ that cover a broad spectrum of science and new technologies, and have the potential to advance understanding and treatment of common diseases – including diabetes, anemia, corneal and other eye diseases, and chronic skin ulcers – as well as rare diseases, including idiopathic pulmonary fibrosis, inherited skin diseases, and sickle cell disease.

Several awards will explore the use of adult stem cells to make specialized cells and tissues that could help reduce the need for whole organ transplants or otherwise restore normal function. Others aim to develop reliable methods of generating platelets and optimizing red blood cell production in the lab to improve the safety and supply of blood available for transfusion.

To inform future funding decisions, NIH and FDA hosted a workshop in December 2017¹⁴ to explore the state of regenerative medicine science involving adult stem cells, with a focus on promising approaches for the development of safe and effective products, scientific areas poised for major transformative advances, and critical gaps that must be addressed to enable significant innovation and rapid advancement of the field. A Funding Opportunity Announcement for new awards will be issued in FY 2018 and we anticipate the remaining authorized RMIP funds (\$28 million) will support up to 15 projects, including both late-stage pre-clinical studies and early-phase clinical trials.

¹³ <https://www.nih.gov/rmi/fy-2017-funded-awards>.

¹⁴ <https://www.nih.gov/research-training/medical-research-initiatives/cures>.

In addition, we are establishing a collaborative network of entities, an “RM Innovation Catalyst,” to provide much needed clinical services to support RMIP awardees, including in-depth stem cell characterization, support to address regulatory requirements, manufacturing assistance for preparation of clinical grade stem cell products, and storage and sharing of clinical data. NIH looks forward to the opportunity the Cures Act provides to significantly advance this field of science.

Conclusion

Thank you for your leadership and dedication that resulted in enacting the Cures Act 18 months ago. The Cures Act has provided NIH with critical resources and tools to advance our mission – to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. We appreciate Congress’s support for NIH through the Cures Act and will continue to implement the law to accelerate scientific discoveries and develop new approaches to the prevention, treatment, and cure of disease.

Mr. BURGESS. Thank you, Dr. Collins.

Dr. Gottlieb, you are recognized for 5 minutes for an opening statement, please.

STATEMENT OF DR. SCOTT GOTTLIEB

Dr. GOTTLIEB. Thank you, Mr. Chairman, Mr. Ranking Member, and members of the subcommittee. Almost 2 years ago, the members of this committee hailed the passage of Cures as a potential game-changer for patients. I agree. I have provided a comprehensive list of our Cures activities in my written statement, but I would like to focus my remarks on one crosscutting priority under Cures, and that is modernizing clinical trials.

FDA has embraced innovative trial designs and novel endpoints in the patient-centered trials envisioned by the Cures Act. Our aim is simple: Innovative, advanced, evidence generation, to assure the timely availability of safe and effective therapies. The Cures Act is catalyzing these approaches and catalyzing the development of new precision medical technologies that are enabling us to target, arrest, and cure intractable conditions. These advances aren't cheap. Access and cost is a big issue.

And I know some question whether our market base system for medical innovation is financially sustainable. They ask if we can afford this coming wave of precision-guided therapies. I would say, we couldn't sustain our system without them. New advances, like regenerative medicine and gene therapy, can displace costs associated with serious illness by restoring function and reducing reliance on costly medical care delivered in hospitals and nursing homes. The best solution isn't to reduce market incentives for innovation, but to make it easier to bring new innovations and competition to the market, all without compromising one bit FDA's rigorous gold standard for product regulation.

That brings me back to modernizing clinical trials. Rising trial costs and complexity undoubtedly impacts market competition and drug pricing. It can be a barrier to getting timely competition to newly approved branded innovative drugs. One reason we may be seeing higher costs is because it is taking longer for competition to emerge in some of these categories where specialty drugs are targeting unmet medical needs. We studied this question at FDA, and the data confirms these trends. I want to share a snapshot today of what we found. We plan to publish the full results really soon.

For nonorphan drugs that treat conditions affecting larger patient populations, 41 percent of the first-in-class drugs approved between the years of 1991 and 2000 had at least one competitor in the same class within 5 years. This rate dropped sharply over the next decade. For the same kind of drugs approved between 2001 and 2010, only 18 percent had a within-class competitor after 5 years.

Another way of interpreting the data is to describe the lag in competition. For the drugs approved in 1991 to 2000, nearly a quarter had a competitor within 2 years. For the cohort of drugs where the first-in-class medicine was approved between 2001 and 2010, it took an additional 5 years for there to be nearly as much competition; and by year 7, competition still lagged, with only 22 percent of the newer cohort of drugs having any competitor.

We see similar patterns in most rare disease treatments as well. These trends mean that costlier branded drugs may enjoy longer periods without facing competition from products in the same class. And this may increase their pricing power. We need to understand why. Part of this has to do with the difficulty of running clinical trials with a second-in-market drug, especially if there is available therapy for a significant unmet need. It is becoming harder and harder to be second, and that is a problem.

Efficient, modern approaches to designing and conducting trials can address some of these challenges and help us get more information about safety and effectiveness at the same time. To advance these and complementary goals, the FDA is pioneering a number of critical advances in clinical trial design.

First, our master clinical trial protocols. These include basket trials, umbrella trials, and platform trials. These approaches can sharply increase trial efficiency and lower costs. They move away from one-drug/one-disease trials and allow the testing of multiple drugs against one or more diseases, or disease subtypes, using a common clinical trial infrastructure.

Another approach is seamless trial designs that compress the traditional three phases of trials into one continuous trial. Through these approaches, you run one continuous trial; and as you enroll new patients, you expand subsequent cohorts of enrolled patients, using the information you learn about the features that help predict benefit from a new treatment.

We are going to be publishing a guidance very soon that lays out how product developers can conduct these seamless trials and how to expand cohorts as trials progress, and a clinical criteria that can be used to expand cohorts as these trials advance. A lot of time and cost of clinical development is spent waiting in between the starting and stopping of the three phases of trials, and seamless trials can compress this.

Every American has already, or will one day, face a serious medical diagnosis, either personally or through a loved one. We need to reduce the burden and the cost of advancing care. The clinical trial reforms we are making today will help ensure more patients who find themselves in these hard circumstances have a better chance of finding a cure, and that market competition helps make these treatments accessible to everyone. Thanks a lot.

[The prepared statement of Dr. Gottlieb follows:]



**U.S. FOOD & DRUG
ADMINISTRATION**

**TESTIMONY
OF
SCOTT GOTTLIEB, M.D.
COMMISSIONER OF FOOD AND DRUGS
FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE
SUBCOMMITTEE ON HEALTH
ENERGY AND COMMERCE COMMITTEE
UNITED STATES HOUSE OF REPRESENTATIVES

"IMPLEMENTING THE 21ST CENTURY CURES ACT:
AN UPDATE FROM FDA AND NIH"**

JULY 25, 2018

RELEASE ONLY UPON DELIVERY

Introduction

Chairman Burgess, Ranking Member Green, and Members of the Subcommittee:

Thank you for the opportunity to testify today on FDA's implementation of the 21st Century Cures Act (Cures Act). A year and a half ago, full Committee Chairman Emeritus Upton and Rep. DeGette hailed the passage of the Cures Act as a potential game-changer for patients. FDA is actively working with industry, health care providers, patients, and many others to turn that bipartisan vision into reality.

The Cures Act sought to catalyze development of new medical technologies at a unique moment in history when fundamental advances in our understanding of the genetic and protein bases of diseases and advances in medical technology have enabled us to target, arrest, and in some cases cure, these vexing conditions.

The law is helping to transform the way we support medical product development and innovation while maintaining FDA's gold standard for safety and effectiveness.

Modernizing Product Development

Revolutionary new medical opportunities require FDA to apply an innovative and nimble, regulatory approach to the products we are tasked with evaluating. I would like to highlight a few central themes of the Cures Act – and describe our approach and recent efforts.

CDER New Drug Program Modernization

FDA recently announced a new drug development modernization plan that provides the structural framework necessary to advance many goals of the Cures Act – and more closely align the scientific prospect of complex and innovative new products with methods and approaches that can best unlock these opportunities.

As part of the modernization effort, FDA's Center for Drug Evaluation and Research (CDER) plans to add review divisions and to organize the divisions more closely around disease types. The proposed changes are intended to free up resources so that our scientists and physicians have more time to focus on advancing the science and technology that can lead to future innovative therapies, particularly to address unmet medical needs. This work requires multiple collaborations with external scientists, expert physicians, patients and other stakeholders to make meaningful progress.

Over a year ago, FDA launched its Oncology Center of Excellence (OCE) to leverage the combined skills of regulatory scientists and reviewers with expertise in drugs, biologics, and devices (including diagnostics). Authorized by the Cures Act, OCE is FDA's first inter-center institute that focuses on a specific disease area rather than type of product.

OCE's interdisciplinary work is yielding significant advances. For example, last May, FDA approved, for adult and pediatric patients, the first cancer treatment based on a tumor's

biomarker rather than the tumor's site or cell type. The immunotherapy was granted accelerated approval and demonstrated efficacy in treating certain solid tumors that progressed following treatment for colorectal cancer and other cancer types. Testing was permitted using a single therapeutic approach for patients with different tumor types rather than requiring separate development programs for each disease site.

In November, using a coordinated, cross-agency approach, the Center for Devices and Radiological Health (CDRH) approved the first breakthrough-designated, next generation sequencing-based in-vitro diagnostic test to identify patients with any of five tumor types who may benefit from 15 different FDA-approved targeted cancer treatment options. OCE supported CDRH's review team in evaluating this innovative testing approach which provides patients and health care professionals with access to critical information in one test report, avoiding the need for duplicative biopsies.

We intend to apply many of the lessons we have learned in creating and operationalizing OCE to break down traditional silos in the development of treatments for other diseases and conditions. Our modernization efforts will deepen internal collaboration and enhance external scientific exchange – and we look forward to updating the Committee on important developments as we move forward.

Novel Clinical Trials

As part of FDA's broader innovation initiative, we are encouraging the use of state-of-the-art innovations such as adaptive trials, modeling, and simulations to allow an evaluation of a product's safety and effectiveness. We welcome early engagement with sponsors to discuss the use of these innovative tools to expedite product development.

Modeling and simulation, for example, play a critical role in organizing diverse data sets and exploring alternate study designs – and can provide a vital tool to help evaluate new treatments in patient population subsets, and for rare diseases where patient populations are inherently difficult to study because of their small size.

CDER and FDA's Center for Biologics Evaluation and Research (CBER) are currently deploying these tools to help predict clinical outcomes, inform trial design, support evidence of effectiveness, and evaluate potential adverse event mechanisms. The Centers are updating guidance to assist sponsors in incorporating modeling and simulation – and applying these tools, for instance, to optimize product dosing based on individual physiology and genetics. CDER is currently collaborating with scientists to develop natural history models in Parkinson's, Huntington's, Alzheimer's, and muscular dystrophy which may facilitate modeling of some aspects of product design and evaluation.

CDRH's scientists and engineers are building in silico regulatory models for product design and evaluation, including the development of a digital library of models and a family of 'virtual patients' for device testing. These tools will enhance consistency across different medical products and across the agency.

Advancing Drug Development Tools

Encouraging the identification and use of reliable Drug Development Tools (DDTs) can significantly advance development of new safe and effective drugs and biologics. The Cures Act revised and codified FDA's qualification process to expedite development of publicly available DDTs, including biomarkers and clinical outcome assessments. FDA is working to establish a regulatory process for qualifying DDTs, pursuant to this codified authority, that provides for timely and consistent review of these submissions. Once qualified, a DDT can be widely used across multiple drug and biologic development programs – facilitating efficient development of important new therapies for patients.

As a result of the Cures Act, and vital resources and commitments provided under PDUFA VI, FDA is placing a greater focus on generation of the data and evidence needed to support biomarker development. Our work is primarily focused in two distinct areas: supporting use of surrogate endpoints in individual drug and biological product development programs, including by cataloguing those previously used as well as a process to develop novel surrogate endpoints; and by facilitating a public process to support biomarker qualification as a drug development tool.

The Cures Act included important provisions for publicly sharing information about DDTs that we believe will help facilitate their development and use. In accordance with the requirements under the Cures Act, FDA will be making a publicly available a list of biomarkers that have been used to support both accelerated and traditional drug and biologics approvals, as well as surrogate endpoints the Agency believes would be acceptable to support approval. While the acceptability of these surrogate endpoints for use in a product development program will be determined on a case-by-case basis, this list is intended to serve as a reference guide to help inform discussions of potential surrogate endpoints with the relevant CBER or CDER review divisions, with the goal of facilitating product development.

We are currently working towards developing and publishing several guidances required by the Cures Act to establish the process, taxonomy, and framework for DDT qualification.

Real World Evidence

The promise of harnessing real world data to improve patient care was an important focus during this Committee's consideration of the Cures Act. We agree that data on every clinical use of a product may provide useful safety and efficacy information.

FDA is actively working to integrate real-world evidence (RWE) such as electronic health records, registries, and claims and billing data into regulatory decision making and to answer questions relevant to broader populations of patients. RWE may go beyond current post-marketing surveillance capacities, eventually becoming applicable across all phases of medical product development.

We are developing a framework to evaluate use of RWE to support approval of new indications of approved medical products, or to help satisfy post-approval study requirements for marketed

products, and are making significant progress in meeting this Cures Act requirement. We have gathered input from stakeholders including industry, academia, and patient advocacy groups. FDA has finalized guidance on the use of RWE for devices, and intends to release guidance on RWE for drugs and biologics.

Although randomized clinical trials are the gold standard for medical and scientific evidence needed to support FDA medical product approval decisions, they are often conducted in specialized and controlled research settings and can be time-consuming and costly. At the end of a development program, randomized clinical trials can still leave critical questions unanswered, particularly about the effects of a medical product after it is used by a broader population over an extended period. We are using powerful new scientific computing and data storage technologies to enhance our capabilities of gaining valuable information from RWE

Sentinel

Sentinel, FDA's national, integrated electronic system for medical product safety, allows continuous feedback on the use of medicines under real-world conditions by providing secure access to multiple data sources, with full patient privacy safeguards.

Within Sentinel, FDA has supported the development of computer programs that analyze health insurance and healthcare provider databases to search for evidence as to whether certain products are potentially associated with specific adverse events, many of which are not typically reported. For example, FDA has used Sentinel to determine whether a certain type of immune therapy is associated with heart attacks or strokes, and to better define the true rate of acute lung injury after transfusions of certain blood components.

The size of its distributed database enables identification of even small exposed populations, and rare adverse events. These investigations can be extended to include comparative studies assessing risk using appropriate adjustments for confounding factors, which is critical when using observational data. In addition, it is possible to perform descriptive analyses of off-label use, appropriate medical product use, medication errors, health outcomes after branded and generic drug use, and product uptake patterns before and after regulatory risk management actions.

Early last year, the Reagan-Udall Foundation's Innovation in Medical Evidence Development and Surveillance (IMEDS) program was launched allowing public and private entities access to Sentinel. Public and private-sector entities, including regulated industry, can now conduct large scale evaluations of safety issues associated with FDA-approved medical products in a secure environment that protects patient privacy.

At the core of IMEDS' innovative approach is the fact that it embraces and enables a long-term partnership between FDA and the public and private sectors. As new tools and methods leave the development pipeline and enter production for FDA use, they also are incorporated into IMEDS. For example, FDA is working to incorporate patient-provided data as well as randomization into the Sentinel infrastructure to support clinical research in a real world setting. Such work could be accelerated through support from sponsors working through IMEDS.

Because it relies on common and transparent procedures and infrastructure that can be understood by all participants, IMEDS appropriately shifts the focus from debates over differing methods and data to the underlying clinical and public health questions of concern.

FDA is confident that IMEDS sponsors will play a key role in shaping the future of evidence generation to help answer outstanding questions about the safe and effective use of medical products in a broad range of populations.

The National Evaluation System for health Technology (NEST)

The National Evaluation System for health Technology, or NEST is a multi-stakeholder collaboration that supports the generation of more and better RWE about medical devices. NEST is designed to drive down the time and cost of bringing new devices to market, expand indications for already marketed devices, and improve surveillance of marketed devices. NEST will enable faster identification of safety issues, reducing harm to patients and enabling companies to more rapidly take any appropriate corrective actions. NEST can also be used by device manufacturers, patient groups, hospital systems, insurance providers, and others to provide data to support those groups' activities.

When fully functional, NEST will improve active surveillance by providing a tool for utilizing real world data rather than only passively relying on patients, physicians, hospitals, and manufacturers to submit information to FDA about suspected or confirmed safety issues. Moreover, the data collected by NEST may help bring safer devices to market more quickly by facilitating the use of more real-world data in approving devices, rather than the current approach of relying solely on clinical trials or bench data, which often represent how devices are used in an ideal setting and may not account for all use cases.

In 2017, CDRH documented access to more than 100 million electronic patient records, and spearheaded the work of 12 National Coordinated Registry Networks and four international Registry Consortia through grants to the Medical Device Epidemiology Network (MDEpiNet), creating infrastructure for device evaluation including minimum core data sets, harmonized definitions, basic governance, and informatics and methodological alignment.

Streamlining Medical Product Review

Since the inception of FDA's first user fee program over a quarter century ago which provided critical resources to supplement product review, FDA has dramatically reduced review time for new, safe and effective medical products. We are consistently meeting product review goals -- many in abbreviated timeframes -- utilizing one or more of FDA's expedited review pathways.

INTERACT Early Meeting Program

Recognizing that early discussions with developers can advance product development, CBER recently established a new meeting program: INitial Targeted Engagement for Regulatory Advice on CBER products (or INTERACT). The INTERACT meeting program was created for potential sponsors to engage with CBER staff and obtain advice on a specific topic or issue that is critical to early product development. These discussions can help answer important questions,

remove roadblocks, and ultimately help create a clearer route to getting safe and effective products to patients.

Device Program

Congress, in the Cures Act, sought to promote medical device innovation and improve patient care. Since medical device technology evolves quickly, the process for improving the performance and clinical characteristics of medical devices is highly iterative. Often, small modifications provide incremental but meaningful improvements to products. Over time, these cumulative changes make noticeable advances in the performances of different technologies. Innovators need the flexibility to efficiently make these kinds of small modifications. At the same time, FDA needs to establish modern tools and benchmarks for measuring the safety and performance of devices to make sure they are delivering the expected benefits to patients.

FDA has embraced the concept of least burdensome regulation as clarified and expanded in the Cures Act – and CDRH has made it a guiding principle for medical device regulation. In just the past few years, we have seen notable results including reduction in review times and improved quality of applications.

As an example of CDRH's least burdensome approach, the Center used streamlined authority provided in the Cures Act, to exempt more than 70 Class I device types and 1,000+ Class II device types from the requirement to submit a 510(k) following a determination that premarket review is not necessary to provide a reasonable assurance of safety and effectiveness. These medical devices may be subject to other regulatory controls, including complying with current good manufacturing practice requirements, being suitable for the intended use, being adequately packaged and properly labeled, and having current establishment registration and device listing with FDA. Eliminating the 510(k) requirement for these products saves time and resources for industry and allows FDA to focus its oversight on higher risk products while still ensuring that patients have access to safe and effective medical devices.

Digital Health

From mobile medical apps and fitness trackers to software that supports the clinical decisions doctors make every day, digital technology has been driving a revolution in health care. FDA recognizes that it can help encourage digital health innovation by making its policies and processes more efficient and modernizing its regulatory tools. The Cures Act codified into law many of the policies FDA had instituted in the years preceding the Cures Act and excluded certain digital health software functions from the statutory definition of a “device,” thereby removing them from regulatory oversight as devices. Such functions tend to be low risk but can provide great benefits by enabling patients and consumers to be more informed and engaged in their health.

In July 2017, FDA issued a Digital Health Innovation Action Plan to fully implement the provisions of the Cures Act that do provide for regulatory oversight of software, including issuing new policy on clinical and patient decision support software, establishing a dedicated Digital Health Unit in the FDA's medical device center supported by industry user fee funding,

and implementing a new regulatory model for digital health technologies consistent with International Medical Device Regulators Forum (IMDRF) policies.

In a Digital Health Software Precertification (Pre-Cert) pilot program, FDA is also exploring a potential voluntary pathway to assess the safety and effectiveness of certain software device products by focusing on the software manufacturer/developer, rather than primarily the product. Under this potential framework, software developers could be assessed and precertified for the quality of their software design, testing, and other appropriate capabilities to qualify for a more streamlined premarket review process or in lieu of premarket review. This firm-based approach differs from the agency's traditional reliance on individual product reviews and seeks to leverage real world evidence to support evaluations of safety and effectiveness. The goal of this pilot program is to collaboratively explore this potential framework. FDA continues to assess its current statutory and regulatory authorities for this program.

New Expedited Review Programs

Congress, in the Cures Act, also authorized an expedited device review pathway, and two important, expedited review programs for drugs and biological products intended to treat serious diseases or conditions. They include the Regenerative Medicine Advanced Therapy (RMAT) designation program and the limited population pathway for antibacterial and antifungal drugs (LPAD). Each is described in greater detail below.

Breakthrough Devices Program

Through the Cures Act, Congress built on and expanded FDA's successful Expedited Access Pathway (EAP) program in the Breakthrough Devices provisions. The Breakthrough Devices Program is a voluntary program for certain medical devices that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions. It is intended to help accelerate patient access by expediting development, assessment, and review of these devices, while preserving the statutory standards for marketing authorization, consistent with the agency's mission to protect and promote public health. For Breakthrough Devices, sponsors generally have earlier and more frequent access to FDA staff during device development and review.

Since the EAP program's inception, FDA has designated 72 devices as breakthrough and authorized the marketing of six. Among those products was a brain implant for patients with blindness caused by damage to the optic nerve. The product mimics the perception of light through a miniature video camera worn by a patient that transmits signals to an implant in their visual cortex. The Breakthrough designation facilitated early interactions between FDA and the sponsor and brought together intra-agency specialists to pose questions, solve problems, and evaluate the benefits and risks of the device for which no standard existed.

Regenerative Medicine

One of the most promising new fields of science and medicine is cell therapies used in regenerative medicine. These new technologies, most of which are in early stages of development, hold significant promise for transformative and potentially curative treatments for some of our most troubling and intractable medical maladies.

The Cures Act recognized these opportunities by building on FDA's existing expedited programs available to regenerative medicine products and by authorizing the Regenerative Medicine Advanced Therapy (RMAT) designation program. CBER moved quickly to establish the RMAT program which aims to facilitate an efficient development program, expedited review of innovative therapies, and more timely access to potentially life-saving products. Products granted RMAT designation are eligible for increased early interactions with FDA, including all the benefits available to breakthrough therapies. As of June 30, CBER has granted 24 RMAT designations since the program's inception.

In the fall of 2017, FDA announced the agency's Comprehensive Policy Framework for Regenerative Medicine. The framework clarifies the agency's current risk-based, flexible regulatory approach and implements provisions of the Cures Act related to regenerative medicine through a series of guidance documents which, when finalized, will represent the agency's recommendations and position on these matters. The first draft guidance document addresses expedited programs for regenerative medicine therapies, including the new RMAT designation program, while the other addresses devices used in recovery, isolation, or delivery of RMAT products.

In particular, the draft guidance on expedited programs describes regenerative medicine therapies eligible for RMAT designation as including cell therapies, therapeutic tissue engineering products, human cell and tissue products, and combination products using certain such therapies or products, as well as gene therapies that lead to a durable modification of cells or tissues (including genetically modified cells). For example, Chimeric Antigen Receptor T-cell (or CAR-T) products, have been considered by FDA to be a form of gene therapy, and RMAT designation is available to CAR-T products that meet the other criteria for designation.

CBER is also working to implement another important regenerative medicine-related provision of the Cures Act. Through a public process involving outside stakeholders, CBER is working to advance the development of standards and consensus definitions to support the development, evaluation, and review of regenerative medicine therapies and regenerative medicine advanced therapies, including the manufacturing processes and controls of such products.

In 2017, CBER approved three gene therapies, one of which was the first *in vivo* gene therapy approved, as well as two CAR-T *ex vivo* gene therapies for oncology indications. Earlier this month we unveiled six new draft guidance documents, which, when finalized, will advance the development of gene therapy products. Three draft guidance documents focus on rare diseases and two specific therapeutic areas: hemophilia and retinal disorders. These draft guidances suggest potential accelerated approval endpoints for certain gene therapy products. The other three draft guidance documents address specific manufacturing and clinical issues related to gene

therapy products. By providing clarity to developers on manufacturing parameters, safety measures, and the pathway toward clinical development, we hope to foster even greater innovation in this field.

Gene therapy was largely a theoretical promise a few decades ago. Now, there is a real possibility that these products will cure diseases. The field is moving ahead rapidly, and our FDA scientists are focused on addressing the challenges in manufacturing and clinical development that arise.

Advancing Antimicrobial Development (Limited Population Pathway for Antibacterial Drugs)

More and more bacteria are growing resistant to currently available antibacterial drugs. Members of this Committee were instrumental in providing additional tools in Cures to further tackle this serious public health threat. Several provisions of the Antibiotic Development to Advance Patient Treatment (ADAPT) Act were enacted as part of the Cures Act, including authorization of the limited population pathway for antibacterial and antifungal drugs (LPAD) to spur drug development in this area. The LPAD pathway is designed to facilitate development and approval of antibacterial and antifungal drugs intended to treat serious or life-threatening infections in a limited population of patients with unmet need. In certain circumstances, the LPAD pathway will be an important tool enabling FDA to conclude that the benefits of a drug outweigh its risks in the intended limited population.

In June, FDA published draft guidance describing the recommended criteria, processes, and other general considerations for demonstrating the safety and effectiveness of drugs approved under the LPAD pathway. We are actively reaching out to discuss the availability of this pathway within the scientific and policy community involved in antibacterial drug development, are working with drug sponsors who are interested in utilizing the LPAD pathway, and look forward to further refining the pathway in the months ahead, as the guidance is finalized.

Last December, FDA launched the susceptibility test interpretive criteria (“breakpoints”) webpages also required by the Cures Act. The Cures Act clarified FDA’s authority to remove the breakpoint information from antimicrobial drug labeling, leverage the work done by standards development organizations, and take advantage of online tools to modernize and streamline the updating of breakpoints information for these antimicrobial drugs. The breakpoints webpages are an integral part of these efforts. Laboratories and antimicrobial susceptibility testing (AST) device manufacturers need to be able to use up-to-date breakpoints for the reports provided to physicians to inform appropriate treatment choices. Up-to-date AST results also are used to determine when additional infection prevention measures need to be implemented to prevent the spread of resistance microbes.

Elevating Patient Voices

Consistent with the Cures Act, FDA is also actively working to elevate patient voices in developing new medical products to treat their diseases. We learn through scientific advances, but also by listening to patients. We must make the science of medical product development and review more modern and more patient-centered, so that approved products successfully address the aspects of disease that concern real-world patients and families the most.

Patient-Focused Drug Development

Through the Patient Focused Drug Development (PFDD) initiative, started as part of the commitments under the Prescription Drug User Fee Act (PDUFA) V, FDA has been addressing the need to better enable patients to provide meaningful input into drug and biologic development. To date, FDA has led more than 20 PFDD meetings to learn from patients impacted by diseases, including, autism, HIV, Parkinson's disease, and various conditions involving pain. These meetings have given the FDA's professional staff a deeper understanding of patient and caregiver experiences.

Our PFDD efforts have been important in helping to address the opioid crisis. While we work to ensure the appropriate prescribing of opioids, we remain focused on striking the right balance between decreasing exposure to opioids and ensuring that those who are suffering from chronic pain have access to treatment for their legitimate medical needs. We also continue to support the exploration of new treatments for both pain as well as addiction.

We recognize the need to engage the wider stakeholder community and provide guidance on approaches to bridge early-stage efforts, such as PFDD meetings, to more systematic, methodologically-sound approaches to collect patient input that can further inform regulatory decision-making.

In June, FDA issued the first of four methodological PFDD guidance documents required by the Cures Act. Taken together, when finalized, the guidance documents will address, in a stepwise fashion, how patient experience data and other relevant information from patients and caregivers can be collected and used for medical product development and regulatory decision-making. The first draft guidance addresses sampling methods for collecting representative information on patient experience to inform the development and evaluation of medical products throughout the medical product lifecycle. It also discusses methods to operationalize and standardize the collection, analysis and dissemination of patient experience data.

We will continue to build on these efforts. The Cures Act identified patient-focused drug development as a priority, and PDUFA VI made it a centerpiece by providing essential resources. As the nature of drug development becomes more targeted and as more of the new treatments address specific aspects of disease, our approach to development and regulation must also become more patient focused. Through the input we receive from the patient community, we can bridge this critical gap between the science and the needs of patients.

CDRH is also committed to partnering with patients. While the Cures Act did not include mandates related to patient engagement for devices, CDRH has been a leader in incorporating patient preference information (PPI) into regulatory decision-making, including by championing patient reported outcomes (PROs). We appreciate Congress' and industry's support for our patient engagement activities in the MDUFA IV reauthorization, including funding to support increasing our capacity to evaluate PPI and PROs in premarket submissions.

Other Actions Under the Cures Act

There are other activities FDA has undertaken to implement the Cures Act provisions, which will lead to greater support for medical innovation and development. These activities are spearheaded by offices other than the medical product Centers.

We are grateful that Congress recognized that the expertise of FDA's staff is essential for maintaining the high quality of our work and therefore included new human resource (HR) authorities for FDA in the Cures Act. These authorities give FDA the ability to simplify and expedite the hiring process for certain positions, and grant new pay authority so FDA can better compete with the private sector to recruit and retain outstanding, highly qualified individuals for these positions. The ability to maintain our outstanding workforce will strengthen FDA's ability to realize the Cures Act goal of accelerating the development and availability of innovative, safe, and effective medical products for patients.

FDA has implemented the Cures Act provision authorizing the establishment of a material threat medical countermeasure priority review voucher program to encourage the development of medical countermeasures. FDA recently approved the first drug with an indication for the treatment of smallpox and awarded the first Material Threat Medical Countermeasure Priority Review Voucher in conjunction with this product approval. Collaborative work continues with other agencies within HHS to address research needs in drug development involving pregnant and lactating women, to streamline regulatory requirements for research involving animals, and to harmonize human subject protection requirements.

Conclusion

These are just some of the ways the Cures Act has supported and enhanced FDA's work to further benefit patients and affirm our nation's standing as a global leader in biomedical innovation.

Thank you for the opportunity to discuss our early progress in meeting the Cure's Act requirements and goals. I look forward to continuing to work with the Committee as we build on these successes and work to achieve its underlying goals. I am happy to answer any questions.

Mr. BURGESS. Thank you, Dr. Gottlieb.

And, again, thanks to all of our witnesses for agreeing to be here. We will now proceed to the member question-and-answer part of the hearing, and we will still yield to Chairman Walden when he comes in for an opening statement. But let me recognize myself 5 minutes for questions.

Dr. Collins, thanks for being here. Thanks for bringing your backup. So let me ask you a question. On the 21st Century Cures, we tried to identify ways to get regulations and policies that were inconsistent, and to give you some flexibility to move past some of these that are overlapping and unnecessarily duplicative to relieve some of the administrative burden. I think the Act asked you to review that.

So can you, perhaps, share with us where you are in the review and how NIH has identified some opportunities to relieve the burden on investigators?

Dr. COLLINS. Yes, I am happy to do so. And, again, thanks to the committee for making all of those changes part of this bill. Some of them may seem kind of bureaucratic and administrative, but they make a huge difference to us in terms of the ability to carry out our mission.

We have been asked, for instance, to look at the way in which we have asked our grantees to deal with financial conflicts of interest, which we think are very important for us to track, but where the mechanisms for doing that tracking were seen as unduly onerous. And we are in the process of going through that with our colleagues at HHS, and I think there will be some changes that will make that a more efficient process.

Another thing, again, that sounds pretty down in the weeds, but it mattered a lot to us, is the degree to which we need to do monitoring of what you would call a subrecipient, where you give a grant to a particular institution, and then they have a subpart of that to another individual. And in the past, our need to reach through and do very detailed monitoring, even of subrecipients, was something that we were required to do without a whole lot of reason for that. And so we have already moved to simplify that process.

Financial expenditure reporting, a lot of the reports that have been done in the past produce data that not very many people look at, and yet at the same time, we need to be sure that we are being good stewards; and that is also being simplified.

We are looking right now at animal care and use, and the oversight that is necessary, of course, to be sure that we are dealing with animals in an ethical way. But some of those particular oversight mechanisms are now being reviewed, and we put out an RFI and got 19,000 comments back from people who have opinions about how we might streamline this process.

Those are a few of the examples. Again, it was really helpful having those features into 21st Century Cures to give us the authority to do those things.

Mr. BURGESS. And obviously, ongoing, it is going to be important for us to communicate on this, and if there are ways where we can provide additional legislative help on that, I think you would find the committee willing to have those discussions.

Dr. COLLINS. Thank you.

Mr. BURGESS. Dr. Gottlieb, thank you for your comments on the clinical trial reform. And I always felt while we were doing the roundtables for Cures, that that is likely where the big money was. If we could reduce the time in trial, if a product was going to fail, allow it to be identified and fail early so we didn't spend a lot of time chasing something that was not going to pan out.

So I really like the concept that you just elucidated about the seamless trial concept and condensing the time between Phase I, Phase II, and Phase III clinical trials. I think that is likely to have a significant impact.

One of the things that has always concerned me is that we have had some legislation, there has been a little controversy, but the ability for all—we don't have a payer here, we don't have CMS, but for the researcher, the regulator, and the payer to communicate before something comes.

I always got the impression that when Hepatitis C, when SOVALDI came down the pike, that the payers at the State level, certainly the Medicaid payers, were not ready for what was happening, but they had been prohibited from having those discussions because of current law.

So I am hopeful that we are able to do something, because particularly in gene therapy or gene editing, rather, where you have one shot that is going to cure something that is a lifelong problem, that is huge, but it is likely to be priced out of the range of most average people's budgets.

Can you comment on that, on our ability to communicate prior to approval?

Dr. GOTTLIEB. Thank you, Mr. Chairman. I think we, I would say, fully addressed this issue. And your points are well-made, and I share your concerns and have shared your concerns in the past. I think we have fully addressed this issue with the guidance that we issued earlier this year. That was, in part, built off of a Cures provision related to payer communications with product developers for purposes of engaging in value-based contracting and other economic kinds of discussions, where we have essentially established a safe harbor for those kinds of communications where the FDA isn't opining on whether or not it has the legal authority to provide any regulation to that context, and some would argue we don't on First Amendment grounds. But even if we did, we would not choose to exercise that authority because, as a matter of public health, we believe there should be robust discussions between product developers and payers for the purposes that you suggest, so they can engage in value-based contracting, other novel ways to try to pay for these very novel therapies.

Mr. BURGESS. Great. Thank you. Thank you for that answer.

I yield back my time and recognize Mr. Green, 5 minutes for questions, please.

Mr. GREEN. Thank you, Mr. Chairman. And, again, I welcome our whole panel here.

Let me give an example of what has happened in the last 4 years. In 2014, we had an outbreak of Ebola in West Africa. There was no treatment for it. And today, what we are seeing in the Democratic Republic of Congo, we have a vaccine. What has hap-

pened in those 4 years? Now, Cures came on in 2016. But can Dr. Collins or Dr. Gottlieb share that? How did that become? I know Merck actually has the vaccine now, but how did we get there? Because back in 2014, there was no vaccine.

Dr. GOTTLIEB. I will let Francis talk, because the vaccine came from him, and I will comment on where it is now.

Mr. GREEN. It has to be approved.

Dr. GOTTLIEB. Exactly.

Dr. COLLINS. So NIH actually began working on an Ebola vaccine back in the 1990s, when nobody had really paid that much attention to this, but we were concerned that this might, at some point, become important. So there was already a fundamental amount of basic science and work toward a vaccine happening for a good 15 to 18 years before the crisis that struck in West Africa in 2014.

That being the case, this was, in fact, a program that developed a vaccine in record time, but still not, in fact, for West Africa in time to have much of an impact on the actual outbreak, because by the time the vaccine was being distributed, good public health measures were already resulting in the epidemic waning rather quickly, which was a good thing.

With the DRC, this vaccine, which is manufactured by Merck, but based upon a close collaboration with NIH—in fact, the Phase I trials for this very vaccine were done in the NIH Clinical Center up here in Bethesda, showing that it was, in fact, safe and seemed to generate good antibody titers. That was distributed in DRC in a ring vaccination strategy, and also giving them to healthcare workers.

And we were very happy to see yesterday, the declaration that this epidemic is now over. Did the vaccine contribute to that? It is a little hard to tell, because, fortunately, this was a limited outbreak. DRC moved quickly with traditional measures. But I think, again, we are very well-situated now to deal with an Ebola outbreak in the future. In this instance, it was great to see how quickly the vaccine was available, got distributed, and was made available to those who needed it.

Dr. GOTTLIEB. I will comment just to build off Dr. Collins' comments. I make two points up front: First, I think it is hard to understate what a game-changer this is. This is the first time that we now have a technology available in the setting of Ebola to intervene to stop the spread with something other than just traditional public health tools of isolation.

I also think we should make note of the efforts of the manufacturer in this case, Merck; the doses that were deployed in the DRC were donated. They shipped about 13,000 doses to WHO. WHO handled the transport to the DRC. It was delivered under an expanded access protocol that was administered by the WHO. So this was very much an altruistic effort that helped in that setting.

I will say that we are working efficiently to try to move toward a licensed product here in the U.S. Obviously, I need to be cautious what I say, but I feel optimistic that this will be something that we can accomplish in the near term, and we can have a fully licensed vaccine.

Mr. GREEN. Well, and that is just an example, because we had a gentleman from West Africa come to Dallas, Texas, and the pro-

protocols weren't followed, and so it impacted our own country. But using this as a paradigm on what we can do for other terrible illnesses that are developing, and I tell people on any given day, we have tuberculosis in the city of Houston, because it is an international city, and you just don't check everybody. So we have to be on our toes to be able to do that.

And the 21st Century Cures, I think, gives you some focus. But looking at the Ebola vaccine, in 4 years, we went from people worried it is going to get—and I was trying to explain to folks, more of my constituents will die of the flu because they didn't get a flu shot than will ever be exposed to Ebola. And we want to keep it that way, though.

But I am concerned about the growing threat of the antibiotic resistance, and that is why I sponsored a provision in 21st Century Cures to create a pathway for these antibiotics that would meet unmet medical needs. The provisions directed FDA and CDC to coordinate efforts with respect to monitoring antibiotic resistance, and any other drugs approved under the limited population pathway for antibiotic and antifungal drugs.

Dr. Gottlieb, what steps has the FDA taken to coordinate with the CDC to support policy that promotes judicious antibiotic use and antibiotic stewardship?

Dr. GOTTLIEB. We have taken a number of steps. We are going to be taking some additional steps to look at antibiotic use in animal feed, the length, the duration of use and the indications in which they are used, and plan to have some additional policy steps that we should be announcing within the next couple of months to continue to advance what we have already done in that regard to reduce the use of antibiotics in animal feed and limit one route by which we are seeing the resistance develop.

And as well, with both the provisions in FDASIA, the QIDP, Qualified Infectious Disease Product provisions, as well as the LPAD that was also enabled in legislation passed by this committee, we have been able to create new pathways to try to provide additional incentives and additional efficient pathways to get new drugs to the market that attack some of these multidrug resistant pathogens.

I would just close by saying I think it is still important that we focus on trying to develop new pull incentives and new ways to potentially reimburse some of these limited-use anti-infectives as a way to create additional incentives for the development of these products.

And we are working on one such idea in conjunction with our colleagues at CMS to try to move towards a different reimbursement paradigm for drugs that are the kinds that you want to just put on the shelf and never have to use, moving toward a site licensing model as opposed to a pay-per-use model, which has been the traditional way that we have paid for drugs.

Mr. GREEN. Thank you, Mr. Chairman. I know I am way over time and I will yield back the time I don't have.

Mr. BURGESS. The chair thanks the gentleman.

The chair recognizes the gentleman from Kentucky, Mr. Guthrie, the vice chairman of the subcommittee, 5 minutes for questions please.

Mr. GUTHRIE. Thank you, Mr. Chairman.

I have a couple of questions, but first I want to say I know there is a lot going on in this great city and this great country moving forward. And a lot of times what is happening in this hearing—a lot of hearings make television. This one probably doesn't make a lot of prime time television, but it is important. It is extremely important what happened when a bill like the 21st Century Cures passed, I think got a voice vote out of this committee, overwhelmingly bipartisan, and really makes a difference in people's lives.

And, Dr. Collins, you and I had a meeting the other day with a member of the band, U2. I only point that out because he was talking about somebody that was close to him that had had childhood cancer. And I remember walking away, because I had a friend of mine that passed away when I was about 11 or 12, and she would be alive today if she had the same disease this time, or probably would be alive today. And the reason I point out U2, because I think they, being Irish, really love this country and they really point out why America inspires the world and does things throughout the world.

And people throughout the world do research, but nobody compares to what you are doing at NIH, what we are doing as a country, what our healthcare system, what our industry, public-private partnerships. And it is just a shame that—the old Annie Murray song, We Could Use a Little Good News Today. There is a lot of good news, and a lot of it is happening in what people and this panel is doing. We really appreciate it very much.

But I do have a couple questions for Dr. Gottlieb. One is specific on the Cures Act. It codified many practices in the Office of Combination Products, but also included provisions to clarify regulatory requirements, improve processes. Can you explain how the FDA is delivering on these efforts in the complex area of regulation?

Dr. GOTTLIEB. We have put forward a number of additional guidances as well as staff manual guidances on how we approach combination products in the agency. Historically, it has been challenging for the agency. I think we have made a lot of progress in recent years. I think we have made a lot of progress owing to some of the provisions that flow out of the Cures Act as well.

We set up a Combinations Council to try to adjudicate who has primary jurisdiction over these products, and we will be putting out a guidance sometime probably this fall, end of the summer, early fall, that is going to make some further process reforms that I think is going to make it more efficient for products that sit on that cusp to move into the device realm, which I think is the preferred route for a lot of product developers, if they can get there.

So we are going to look for ways to find the most efficient route while being mindful of our public health obligations in these circumstances.

Mr. GUTHRIE. Well, thank you. And also, you and I talked just recently on the telephone, and several of us here sent a letter concerning drug shortages, drug supply shortages. I know I have had an emergency room physician from my district say that sometimes they don't have just the simple things they need. They have to be more creative. They have to figure out other things to move forward.

I know some of it was tied to the natural disaster in Puerto Rico. I think you guys really went in and handled it. That is what people need to know. There are people in government that are trying to make things work. We have issues we need to address. But what happened in Puerto Rico to get pharmaceuticals moving again, what you guys have done. But I know there are still issues with drug shortages. I hear from EMS, emergency room physicians, anesthesiologists, just basic things.

Could you just talk to me about a minute and a half what you explained to me on the phone and what you are doing with your Drug Task Force and what is pressing and what is moving forward?

Dr. GOTTLIEB. So the challenges here are structural in my view, Congressman. If it is not one thing in shortage today, it is going to be another thing tomorrow. And we are dealing specifically with sterile parenteral drugs, the sterile injectable drugs, and those are the ones that seem to be chronically in shortage.

I think there are structural problems in that. Frankly, reimbursement has been driven down so low. Many of these drugs are manufactured slightly above cost of goods. So the only way to profitably manufacture them is to do it at tremendous scale. So we have seen a lot of consolidation in the space, but we have also seen underinvestment in manufacturing, because there aren't a lot of margins to reinvest in manufacturing.

And I will say manufacturing these isn't trivial. It is one thing to manufacture a small-molecule drug and have a margin that is slightly above cost of goods. It is quite different when you are trying to manufacture a sterile, injectable drug. So things go wrong, and when things do go wrong, since this space is consolidated, if one facility gets shuttered it could take down 30, 40 percent of the market.

We think there are things we can do, apply an additional regulatory touch to some of these critical drugs, if we could define sort of a category of what we would say are critical access drugs that we don't want to go into shortage. But, quite frankly, I am concerned that my regulatory touch is only going to exacerbate the problem insofar as it will increase cost.

So what we are trying to do with our shortages task force is look at this holistically, and bring in our colleagues from the VA and CMS and look at how we might couple some additional regulatory steps that we could take to mitigate shortages, or try to prevent them with some potential changes in the reimbursement structure for certain of these drugs.

We talk a lot about drugs that are priced too high. And there are drugs that are very costly, and probably exceed the value that they are delivering. But there are drugs also that probably are priced too low relative to their importance and the cost of manufacturing them. And I think we need to take another look at how we reimburse these old sterile, parenteral generic drugs, off-patent drugs.

Mr. GUTHRIE. Well, thank you very much. And my time is expired and I yield back. Thank you all for being here.

Mr. BURGESS. The chair thanks the gentleman. The gentleman yields back.

The chair recognizes the gentleman from New Jersey, Mr. Pallone, the ranking member of the full committee, 5 minutes for questions, please.

Mr. PALLONE. Thank you, Mr. Chairman.

First, I have a question for Dr. Gottlieb, and then I want to go to Dr. Collins for a second one.

Last week, FDA announced the release of its biosimilar action plan, which strives to encourage more innovation and competition in the biologics market. And I believe such action is critical and necessary if patients are to realize the full benefits of biosimilars. While 8 years have passed since the Biologics Price Competition and Innovation Act, only three biosimilars are marketed in the U.S., despite FDA having approved 11 of them. So as you noted yourself, Dr. Gottlieb, competition in this space is anemic.

So I have two questions: First, you are well-aware that the high cost of prescription drugs, including biologics, continues to be a barrier for many patients. As a part of the Biosimilars Action Plan release, you revealed that a recent FDA analysis that found that if all FDA-approved biosimilars were available to American consumers, that significant savings could be realized.

Could you discuss further FDA's analysis and the savings potential that biosimilars could offer?

Dr. GOTTLIEB. I appreciate the question. We are going to be publishing the full results of that analysis soon, but essentially what we did is, we looked at the experience in the European market where we saw product introductions, and extrapolated that experience to what could have happened in the U.S. market if the same product had been introduced in the U.S. market.

So we effectively took the competitive landscape from Europe, made some corrections for the fact that the dynamic in the European market is slightly different than the dynamic in the U.S. market, but looked at the percentage price reductions when one, two, three, four biosimilars entered the market. And when we extrapolated those findings back to the U.S. market, and then assumed that if every biosimilar that was approved in the U.S. market had launched, we extracted that an additional \$4.5 billion would have been saved in 2017.

So the savings are quite significant, and I think, if anything, we probably erred on the side of underestimating them by being very conservative in how we did our analysis.

When you look at the European experience, the savings aren't of the same magnitude that you see in the small molecule world, but they are quite significant. They start to approach the small molecule type of savings once you see four or five product introductions.

Mr. PALLONE. Thanks a lot, really.

The second question, I always want to commend you for your continued dedication to curbing gaming tactics used by certain manufacturers to delay or impede competition, but a question is, how can Congress work with the FDA as you implement the Biosimilars Action Plan to help facilitate greater competition in the biosimilar space?

Dr. GOTTLIEB. I appreciate the question, Congressman. Yes, we are going to look at some of these more difficult scientific questions

that I think could facilitate more competition, like interchangeability.

But one of them, in particular, that we are going to be looking very hard at is being able to use the European product as a reference standard. We have situations where a biosimilar might be manufactured in the same facility and distributed in both the U.S. and Europe. We know that, but our knowledge of that constitutes commercial confidential information. So we have to require a biosimilar entrant to run the study against the U.S.-referenced product, even though the European product is the same thing, and the European product might be cheaper and easier for them to source.

So that there are opportunities, I think, to have cost savings if you could source a reference product globally. And I will add that about half the cost right now of developing a biosimilar—it is highly variable, but, on average, about half the cost of developing a biosimilar are the costs of acquiring the branded biologic to run the trial, to run the comparative trial. So the savings could be significant.

Mr. PALLONE. Thank you.

Let me quickly get to Dr. Collins. You mention in your testimony that NIH is currently building the All of Us data resource, which ultimately help researchers study the data collected from participants and connect to other large datasets. Making this data available to a broad range of researchers obviously has pros and cons, and the two major issues that come to mind are data security and participant privacy.

So let me quickly put two questions into one. Given that NIH is asking participants to share intimate details about their health and lifestyle, how do you plan to ensure data privacy and data security, and are there protocols in place to share updates or study results with participants?

Dr. COLLINS. I am going to ask Dr. Devaney, the Deputy Director, who is all over these issues, to respond to your question.

Mr. PALLONE. Thank you.

Ms. DEVANEY. Thank you for the question and thank you for having us here today.

So we are thrilled about where we have come with the All of Us Research Program. We have over 86,000 participants. Of course, we know, as we try to engage a community of diverse participants, up to a million, or maybe even more, we need to gain their trust. And so privacy is one of our most important priorities.

All of the data that comes into the database source is encrypted and deidentified, and goes into a secure cloud environment. And once we open up access to researchers next year, they will have to abide by a code of conduct, and no data will be allowed to be downloaded from that environment.

In addition, and just really briefly, I want to thank the committee here for giving us really strong privacy protections within the Cures Act, including certificates of confidentiality, which cover all of our data and allow us to really provide robust protections to our participants' confidentiality.

Mr. PALLONE. Thank you. Thank you, Mr. Chairman.

Mr. BURGESS. The chair thanks the gentleman. The gentleman yields back.

The chair recognizes the gentleman from Michigan, Mr. Upton, the author of the Cures legislation, 5 minutes for questions, please.

Mr. UPTON. Well, thank you, Mr. Chairman.

I just want to remind everyone here that this was a great committee process that passed 51 to nothing. And I want to say that everybody that was on the committee in the last Congress actually had a piece of this, because we listened to everybody here. Staff was terrific, that is for sure, but so were the agencies, because you helped lead us to where we wanted to go. The administration. The Senate. We had all the disease groups. We had lots of players, and we appreciated that input.

And I think, based on the hearing today and what we really thought was going to happen, it has fulfilled our expectations, and we have got a lot of time left to play. It is a game-changer. And I got to say, way back when, I was one of the participants with John McCain and Paul Wellstone and Henry Waxman, who doubled the money for the NIH back in the 1990s. The four of us were the sponsors of that bill to get it done. And it was a very important element that we actually increased the money for the NIH, knowing that we had a terrific steward in Dr. Collins, who was going to be able to lead us there.

And I can remember sitting upstairs with Mr. Pallone and Ms. DeGette, my partner, and a few others to talk about how much money we wanted to add to that baseline. And we got it up to a \$45 billion increase over a 10-year span. And the leadership demanded that we have pay-fors for it, and we came up with those not once, but twice, as they were stolen the first time.

And a comment that was made earlier, and it might be more important to have maybe someone from HHS here, but I was too alarmed last week when I read a story that HHS was perhaps re-programming some of the money that we had done a dollar-for-dollar, year-by-year table to make sure that that money went for the NIH.

And I don't know, Dr. Collins, if you have knowledge if there is some truth to the published reports that money was being taken away from what we were able to do and put to something else. I don't know if that is happening. And if it is happening, how do we get it back?

Dr. COLLINS. So I am not aware of the published report you are mentioning. There is, I believe—and we should probably check this—language in 21st Century Cures that prohibits transfer of the funds that are allocated in the Innovation Fund by the Secretary for any other purposes. So I think this is nicely designed so that those funds are intended to go for your original plan.

Mr. UPTON. That is good to hear. I want to talk a little bit about All of Us. And I think privacy protections are important, and it is very important people know about them and that they don't have to worry about that data being stolen. And, as we found, particularly from our roundtables, individuals were more than willing to share what their own experience was, knowing that it was going to protect someone else from maybe having that same ailment.

So it is exciting to hear that 87,000 people have already signed up, really, just in a couple weeks. I know for me, particularly with the privacy protections, we would like to maybe set up a caucus

here, and All of Us caucus that can be bipartisan to encourage members and staff to participate. We have got about, oh, like 25,000 people that work here on the Hill. Maybe we can get a good percentage that will come down to the Gold Room around the corner to figure that out.

I know that researchers are going to have access to this information in about a year or so. How quickly do you think some of that data might be able to be utilized and figure out the right pathway for some real important research to be promising?

Obviously, the news in the last couple weeks about the chemo, and not having chemo for breast cancer was very important, heralded around the country nicely. But how fast do we expect that maybe some of this All of Us information might be able to be used by the researchers with some concrete result of positive?

Dr. COLLINS. Ms. Devaney.

Ms. DEVANEY. Sure. Yes, it is a great question. We are really excited to get some of the brightest minds around the country actually accessing the data. And as you mentioned, 86,000 participants, that data is just going to get richer and richer as we add more participants, and as we get more electronic health record data in on all the participants.

I would imagine that once we give access to researchers, that we would pretty shortly start to see some pretty significant findings. And, of course, the data gets richer with more participants, but over the long term as well, as we get to see people who are healthy, stay healthy, get disease, how they respond to therapies. All of that will be—

Mr. UPTON. Just real quickly, because my time is expiring, how long does it take for someone, if they sign up to do this, what is the time element for them to participate?

Ms. DEVANEY. Sure. So the online enrollment process takes about 45 minutes to go through the consent and to authorize your electronic health record. And then we have the in-person visit where people donate blood and undergo a physical measurement. That takes somewhere between 45 minutes and an hour as well. And then over time, we will be asking participants to continue to fill out surveys and do other things digitally, and maybe even come back for in-person visits over the years.

Mr. UPTON. I yield back.

Mr. BURGESS. The chair thanks the gentleman. The gentleman yields back.

The chair recognizes the gentlelady from California, Ms. Eshoo, 5 minutes for questions, please.

Ms. ESHOO. Thank you, Mr. Chairman.

Good morning, Doctors. It is an honor to have you here. And I can't help but think that while most people in the country don't know our names or what we do, they are all counting on you. So thank you for what you do. I think that you represent part of the real genius of our country. And I always say, NIH stands for our National Institutes of Hope. And you gave us even more hope with your report, Dr. Collins.

Dr. Gottlieb, I know that you are aware that the legislation that my wonderful colleague, Congresswoman Susan Brooks and I wrote, the Strengthening Public Health Emergency Response Act,

was included in the 21st Century Cures Act. And among other provisions, the bill established a priority review voucher to encourage the development of medical countermeasure drugs and vaccines at FDA.

Now, when we developed the bill, the FDA, at that time, expressed concerns that allowing biodefense medical countermeasures to qualify for the PRV, would dramatically increase the number of PRVs awarded. The first product was just approved earlier this month. So does the FDA still have concerns about the number of products that will qualify for the PRV under the legislation? Can you tell us if there has been good interest on the part of companies to apply for it? Can you just maybe briefly inform us about that?

Dr. GOTTLIEB. I appreciate the question, Congresswoman. And I think we all appreciate the effort of this committee to try to provide incentives to these important products. As you noted, the first product that qualified for one of these PRVs was just approved by the FDA. And it is potentially a very important product, a treatment rather than just purely a vaccine for smallpox. The Holy Grail was always to have a treatment in the event of smallpox being used as a bioweapon.

I don't know the position of my colleagues who were here before me, but I certainly wouldn't argue that we have too many medical countermeasures coming into the agency and too many PRVs being issued in this context. I think, if anything, it is probably quite the opposite. We would still like to see more drug development in this realm, and there are still economic challenges to developing these kinds of medicines.

Ms. ESHOO. I appreciate that.

I don't know whether it is Dr. Collins or Dr. Sharpless. Pancreatic cancer is still a death sentence. I did legislation some years ago regarding it. Can you give us an update of if the needle has actually moved? I know when I did the legislation—I can't remember the year—that the needle really hadn't moved in about 40 years. So can you give us just a quick update on that? And then I would like to go to Dr. Devaney for a question.

Dr. SHARPLESS. Sure. I think the answer is yes, the needle has begun to tick ever so slightly up in pancreatic cancer. I was speaking recently at the PanCAN, one of the leading advocacy groups in this space on this topic.

Ms. ESHOO. Marvelous advocates.

Dr. SHARPLESS. They do great work. And I think we have seen some really good stuff. So if you can resect pancreatic cancer, so you get a so-called R zero resection, those patients are doing pretty well. So resectable pancreatic cancer is a minority of those patients, but that group is growing. And we just had a positive trial, a randomized trial announced at ASCO with a significant survival rate for adjuvant chemotherapy in those patients.

Other patients who do not have the RAS mutation, so the so-called RAS wild-type patients, which may be about 10 percent, some of those patients are responding to novel kinase inhibitors, for example, that—

Ms. ESHOO. I think I would like to follow up with you—

Dr. SHARPLESS. Sure.

Ms. ESHOO [continuing]. Because I am not a doctor, so I don't understand everything you just said. But I know that you can break it down for me if we have a conversation or a meeting. I would appreciate it.

Dr. Devaney, thank you for your wonderful report. One of the places where the program is taking place is in my congressional district at the Palo Alto VA. Can you give me just a quick update if you know about the veterans that signed up to participate, how your experience working with the Palo Alto VA? I am very proud of it. It is quite an enterprise there. I have heard from many constituents who were interested, who are interested in participating in All of Us. And I would also like to know how you are advertising to the general public?

Ms. DEVANEY. Sure, yes. I will start with the VA, and—thank you for that by the way—we have a really great partnership with the VA and have for years. And of course they have been running the Million Veteran Program and they have 670,000 veterans or more already enrolled. So we have learned a lot from them.

Dr. Phil Tsao, who is the P.I. at Palo Alto, has been a great partner. They launched a few months ago and have had great success getting veterans enrolled into our program, which has been—it is a really important population for us, because of course the health outcomes that are so important there. And we have also a VA site in Boston. So we are excited to get even more VA sites launched around the country.

Ms. ESHOO. Great and how are you advertising to the public—

Ms. DEVANEY. Sure. Yes. We are using a number of different tactics, learning over time, how do we actually engage across a study that is trying to be national. So we are using different marketing techniques, digital marketing, we are also doing in-person engagement. The healthcare provider organizations, including the VA site, are really critical for us because they have those direct relationships with their patients.

Ms. ESHOO. Thank you very much.

Thank you, Mr. Chairman. I yield back. Thank you again to all of you.

Mr. BURGESS. The chair recognizes the gentleman from Ohio, Mr. Latta, for 5 minutes for your questions, please.

Mr. LATTA. Thank you, Mr. Chairman. And thank you very much to our panel for being here. I really appreciate it and the testimony you have provided. It is important for this country. And also the gentleman from Michigan's not here right now, but I also want to thank him for his leadership on 21st Century Cures and getting us to this point where we are today.

Dr. Collins, if I could start with a question for you in your testimony you talked in regards to the brain initiative. And especially at the end of testimony talking about where it will lead to increased understanding for brain health and a means of preventing brain disorders such as Alzheimer's disease, Parkinson's, Schizophrenia, autism, drug addiction and traumatic brain injury. And I know I also see that there has been about \$1.5 billion that has been allocated over the next 10 years for the studies that is going on, but I know that when I have been at Ohio State and seeing what they are doing with Parkinson's in their studies. But the one

area I would like to focus in on today is on Alzheimer's, because as we look across the Nation today and we are seeing what is happening, and the reports especially from what Alzheimer's association's reports that you are looking at that the cost could rise as high as \$1.1 trillion by the year 2050.

The sixth leading cause of death in the United States today. One in ten Americans over 65 will have it. We have about 5 million Americans living with Alzheimer's today. One-third of Americans over 85 are afflicted with it. But unfortunately, start looking down the road over the next almost 30 years, people over the age of 65 there will be about 14 million people afflicted. Where do you see this going right now with Alzheimer's?

Dr. COLLINS. This is an area of intense interest as a major challenge for the world and certainly that is very true of the United States. You have quoted the frightening numbers of individuals that are projected to be affected and the cost that that is going to apply to our healthcare system.

And even more than that, the personal tragedies that happen every time a diagnosis of this sort appears, it affects not only the individual but their family and the caregivers. We are all in on trying to come up with an aggressive strategy to identify a pathway toward prevention and treatment of the disease. And we are grateful to the Congress because over the course of the last 3 years, Congress has been progressively giving us greater resources to work specifically on Alzheimer's. We are also doing that in a very I think visionary productive partnership with industry in something called the Accelerating Medicines Partnership to try to be sure that the basic science that we are doing on the brain, trying to tell what are the earliest signs of Alzheimer's gets translated quickly into therapeutics.

One of the things we are learning is that Alzheimer's begins long before the first symptom, in terms of cognitive function. And if we are really going to be successful in delaying or preventing it, we need to find people at risk at the earliest possible moment and not wait until they are already in a circumstance of having lost a lot of neurons, because they will be hard to get back at that point.

I am a guardedly optimistic that we are on the right path with some of the trials that are underway right now where we have the opportunity to treat people before they have any symptoms, but we know they are on a dangerous pathway and can watch and see what is happening.

We are also learning a lot more about roles that play a significant hand in what happens with Alzheimer's and the immune system which we hadn't really realized before. And inflammation seems to be important in this condition. And all of the focus that we have had on amyloid and tau, the two proteins that build up in the brain are important, but that may not be the whole story. I could give you a long lecture on this, and I will stop now because of the timetable. But I do want to reassure you that between NIH basic and clinical science working with industry and with close collaborations with the advocates, we are pushing this as fast as we possibly can.

Dr. GOTTLIEB. And I would just add if I may, we work closely with Dr. Collins in these efforts and we recently issued a new guid-

ance document updating the agency's guidance on clinical trial end points in this setting, in this particular disease setting.

Historically there was a perception that you had to show improvement in both functional status and cognition to win approval or at least show that you slowed the decline in functional status and cognition. That is challenging because by the time your functional status declines as an Alzheimer's patient, you probably had a pretty significant decline in cognition.

And now that we are able to identify patients earlier with more sensitive tools to detect changes in cognition, also process prespecify patients who are at high risk of developing Alzheimer's, what we want to do is intervene earlier when there are slight changes in cognition, try to arrest that process. And so what the agency has said is in the right circumstances if you can show an improvement of cognition alone, that could potentially qualify for approval for a drug that would slow the progression of Alzheimer's disease in the right prespecified population that properly identify patients. So we are trying to work closely with NIH as well to help facilitate this innovation.

Mr. LATTA. Thanks Scott.

Dr. COLLINS. That is really important to have that as an end-point.

Mr. LATTA. Well again, thank you very much for our panel. And Mr. Chairman, I yield back.

Mr. BURGESS. The chair thanks the gentleman.

Mr. GREEN. Mr. Chairman, could I ask for the next Member of Congress, Ms. Diana DeGette, could come up and sit in the ranking chair as a cosponsor of the bill.

Mr. BURGESS. No objection.

The gentlelady is recognized for 5 minutes for questions.

Ms. DEGETTE. Thank you so much. I just thought Mr. Green wanted a break. That was very nice of him to recognize me.

And again, I want to add my thanks to all four of our witnesses up here for their extraordinary help, not just in passing this bill, but also in implementing it. It really warms our hearts to see how much progress we have made in such a relatively short time. And it also encourages us to think how much more we can make.

So I just have a few questions for each of our agencies that are here today. I think I will start with the FDA. So Dr. Gottlieb, the biomedical community has really made great strides in developing clinical therapies from a marking of the potential system cells, to creating therapies tailored to the unique genetic fabric of a patient.

And one of the things we have been concerned about for a long time is that overseeing and regulating these cutting edge therapies really requires an experienced, well trained, robust public health workforce.

And so in 21st Century Cures we had a provision for new hiring authorities known as HR Cures. I am wondering if you can talk to us about how the HR Cures authority has helped the agency recruit and retain its talent.

Dr. GOTTLIEB. Thank you, Congresswoman. We are in the process of implementing that. I think it is going to be transformative for the agency in terms of our ability to recruit people with specialized skills. We have identified 38 occupations that meet the re-

quirement for the alternative pay system. We have made the first two hires under the new cures authority, both deputy center directors, but I think this is going to be very important for the agency.

And just to briefly pick up on your point, when we are talking about new treatments like gene therapy and cell base regenerative medicine and even things we are seeing on the medical device side of the house, the clinical characteristics of the products relate very closely to the product features. And the product features change very quickly. The underlying technology of the product itself, these aren't all pills anymore.

Ms. DEGETTE. Right.

Dr. GOTTLIEB. And so it used to be that if you had expertise in the scientific field or the clinical field you could adjudicate all the different kinds of drugs. But now it requires expertise also in the products themselves. The gene therapy platforms, there are regenerative medicine platforms. And we see this a lot on the medical device side of the house where there is a lot of novel technology. You have to have engineering skills on that specific technology. That is where this is going to be particularly helpful, trying to find those people with the very discrete, specialized—

Ms. DEGETTE. These are people you just can't hire someone out of grad school. These are people with really specialized areas of knowledge.

Dr. GOTTLIEB. That is right. And they are people who are often employed in endeavors in the private sector where they are highly paid, highly skilled so we are competing against others for the same small pool of talent.

Ms. DEGETTE. In the FDA June 2018 report called 21st Century Cures Workforce Planning you talk about this patchwork of hiring authorities that have created challenges. Are you beginning to be able to address that?

Dr. GOTTLIEB. We have had historical challenges with the overall hiring framework at FDA going back 15 years or longer. Some of the same challenges that I am grappling with now I saw commissioners grappling with when I was at the agency in 2003 and again in 2007.

We are addressing it very directly. We are trying to do it top down, wholesale change of the hiring process to make it far more efficient. We started a pilot which dramatically streamlined the on boarding process, the hiring process. And we focused that pilot on the PDUFA slots, on the user fee slots. What we have decided to do is basically take that structure of that pilot and apply it to the whole hiring process and not just sort of bifurcate off one set of hiring—

Ms. DEGETTE. I hate to cut you off, but I can't ignore Dr. Collins. And I have about 10 minutes of questions for you, but you are going to have 1 minute to answer them.

Let me just ask you what kind of research is going on over in your agency on alternatives to opioids for pain management? Because the opioid crisis is one of the big issues that has really been facing this committee for the last 1 year or 2.

Dr. COLLINS. Thank you for raising this. This is an incredibly important issue. We are grateful to the Congress that in the omnibus an additional \$500 million was put into our budget to work on the

opioid crisis. And a significant fraction of that is being devoted to just the thing you are raising here, the need to develop affective and nonaddictive pain medicines for those 25 million Americans who suffer from chronic pain every day and for whom opioids is not the answer.

Ms. DEGETTE. Right.

Dr. COLLINS. And actually it is quite harmful in many instances. This goes all the way from basic science, to discovering new targets, to working with industry to help actually free up some ideas that had been on the slow boat and now can be speeded up. Working in a collaborative way. And setting up a clinical trials network so that we can quickly test and see whether new therapeutics that are not addictive work, and in what setting did they work, because all pain is not the same. Low back pain may not be the same as the pain you get from trigeminal neuralgia, and we need to have all ready to go the kind of clinical trial networks that currently doesn't exist.

Ms. DEGETTE. I think, Mr. Chairman, this might be a good subject for a whole separate hearing. Thank you.

Just one last thing, Dr. Gottlieb, I had some questions about some rules that have been pending about shock therapy in the FDA. We don't have time to have you answer those questions right now, but I am going to be contacting your agency to find out why those rules haven't been approved. They have been pending since 2016. And I promised my constituents I would ask you about this so we——

Dr. GOTTLIEB. I would be happy to discuss that with you moving forward thank you.

Ms. DEGETTE. Thank you, very much. Mr. Chairman.

Mr. UPTON. Thank you, Mr. Chairman. I appreciate your holding this hearing. And I want to thank all of our witnesses today and the very talented men and women that you are speaking on behalf of your agencies who do amazing work in the area of healthcare in America Cures. The legislation was passed, medical innovation, reforms to America's and mental health services.

And this is why I thought today was really an important day, an important hearing to continue our work to legislate and evaluate and legislate and evaluate and see what else we need to do going forward. What is working, what is not, and what do we need to change.

I know I have had a lot of roundtable discussions, and hospital board rooms, community centers townhalls with people in my district who are very pleased with the investments we have made in medical research and in turn the work that your scientists are doing.

To turn that money and research into reality, and medicine, and cures that goes from one end of this table to the other. And so we appreciate the work you are doing. A friend in Bend say Carol, who is an MS advocate, has said Cures was a great step toward making it possible to find a cure to MS. And I know you all hear that every day. People are pretty excited about precision medicine, the cures that are out there waiting to be found and the work that you are doing.

Dr. Gottlieb, in your testimony today you suggested there is a correlation between lowering medical product costs and promoting modern clinical trial designs. Can you elaborate on that, because we are all very concerned about the costs of healthcare, the cost of medicines. And clinical research isn't always as efficient as it could be, and how biomarkers and other drug development tools help to make that more efficient in patient centers.

Dr. GOTTLIEB. I appreciate the question, Mr. Chairman. I think while clinical trial costs don't directly translate into how a product is priced, we know that. People price products based on what the market's going to bear and the value that it is delivering. We know that clinical trial costs, cost development costs do factor into the rising costs of the overall development and competitive nature of this landscape. What I talked about in particular today is the complexity of clinical trials, especially in areas of unmet medical need when there is already available therapy is in my view delaying to market the second and third in class drugs.

So these specialty drugs that target unmet medical needs are enjoying monopolies for longer periods of time. And if you believe that subsequent competition and the data shows this is when competition market prices come down, that competition isn't entering and the prices aren't coming down. And we now have data to demonstrate this. We will be publishing that soon. I gave a snapshot of it here today.

I think there are things we can do to try to facilitate more efficient routes to market the second in class drugs and third in class drugs while at the same time increasing our assurance in safety and effectiveness, not sacrificing it one bit. And those are the kinds of development reforms that we are focused on.

Mr. UPTON. And trials for rare diseases can be difficult to conduct, especially if there is already a first FDA approved treatment. How do you spur additional innovation and greater market competition for rare diseases?

Dr. GOTTLIEB. And this gets to some of the changes in the clinical trial designs. One thing in particular is in very rare diseases looking at natural history models to model the behavior of the control arm, or using modeling as simulation, so you don't have to droll placebo trials in those settings, because if there is already available therapy, patients aren't going to want to go on to a placebo if they can otherwise use the available therapy. They are going to want to use an active drug.

So this is a place where we could benefit from more disease models. We should be able to create those. There is a request in the President's budget for about \$20 million which would help facilitate that. I know we have support from this committee and others in Congress for some of those resources so we are very grateful for that. But I think there are things we can do working together.

Mr. UPTON. I appreciate that and a good reminder. The promotion for the President's budget, well done, well played. Send that to the White House.

Drs. Collins, and Devaney, and Sharpless, I saw the NIH recently announced an effort called respond or research on prostate cancer in men of African ancestry defining the roles of genetics, tumor markers and social stress. So that study funded in part by

21st Century Cures Cancer Moon Shot initiative will investigate the environmental and genetic factors of prostate cancer in African-American men. Can you tell us more about this important study and how it will combine molecular approaches in environmental science?

Dr. Sharpless.

Dr. SHARPLESS. Thank you for the question. This is alluding to a trial just announced from the NCI. That will be the largest trial on this topic in our history, so it is going to take 10,000 patients newly collected and 10,000 historical patients and try to analyze the genomes and social factors that contributes to this important disparity. African-American men are likely to be diagnosed with advanced and prostate cancer and are more likely to die of prostate cancer. So understanding this important disparity in our country is really a crucial question and the response trial are exciting.

Mr. UPTON. All right. Anything else anybody want to add?

Dr. Collins.

Dr. COLLINS. I think I just have to point again to the All of Us study as a platform that we will be able to utilize going forward for answering many of that sort. We have this goal and we aim to reach it that about 50 percent of the participants in All of Us are going to come from traditionally underrepresented groups, racial and ethnic groups.

And so if you want to really examine health disparity circumstance, you are going have a million participants who are highly motivated to take part and research on whom we collected a great deal of data. We are going to learn a lot about this kind of health disparity, about all diseases once we have that platform up and going.

Mr. UPTON. Excellent. Excellent. Thank you all. Appreciate your continuing involvement with our committee. It has been positive and effective I think for the American people. And we look forward to doing more together.

And Mr. Chairman, I yield back.

Mr. BURGESS. The chairman thanks the gentleman. The gentleman yields back. The chair recognizes the gentlelady from Florida for 5 minutes for questions, please.

Ms. CASTOR. Thank you, Mr. Chairman. And welcome to all of our witnesses today.

Dr. Collins, I share your enthusiasm over the future of the Cancer Moon Shot in precision medicine. Part of my enthusiasm stems from the fact that back home in Tampa I represent the Moffitt Cancer Center community, the only NCI designated comprehensive cancer center in the State of Florida.

And I love meeting routinely with the young scientists and researchers who now feel like we have given them a new commitment where they were very concerned in the past on the future of NIH funding as it competes with all the other needs. Now they feel like, OK, 21st Century Cures, these new investments for the Cancer Moon Shot, gives them hope for all of their research and the care they are providing.

Dr. Duvaney, the Moffitt Cancer Center has been a national leader in building large datasets, tissue samples before and work-

ing with other institutions, especially for those in underrepresented communities.

You have now given us a bit of an outline on the importance of protecting privacy for the people who participate. Can you tell us a little bit about the protocols going forward for researchers? Will they be required to share their research? When would that happen? Will those research results be available to all for other researchers to build upon?

Ms. DEVANEY. Great question, thank you for that. So, we have been thinking a lot about the—to your point about young investigators, the diversity of researchers also that can access the data, making sure that the platform we are building is open to everyone, and feel responsible for ensuring that the things that we learn on the data, that is so generously provided by our participants, is returned to the scientific community and to our participants in fact.

So we are developing policies around ensuring that researchers who access the data required to follow code of conduct and share their results within a specific amount of time. And we are still finalizing those policies in anticipation of opening up the data next year, and policies around returning results back to participants who participate in the study as well.

Mr. COSTELLO. Because Dr. Collins, in the past it has been kind of siloed. If certain researchers had kind of kept it, held it close, and didn't make all the data available, what does the future hold do you think?

Dr. COLLINS. I appreciate the question. And I appreciate 21st Century Cures gave me, as the NIH director, authority, that I did not have before, to require data access for studies that we support. I could cajole in the past. I could try to embarrass people, but I didn't really have the clout to say, this is a requirement. If you are getting a grant from NIH, you are required to make your data accessible.

You all gave me that and that has been a very useful tool. And we are very engaged in the process of trying to establish exactly what that needs to look like for a wide variety of studies. We have done it particularly for genomics where we have a very well worked out genomic data sharing policy, and we are in the process of working that out for things like imaging and electronic health record information and so on. But this is a very high priority. We hate those silos too and we have been having a good time knocking them down.

Ms. CASTOR. Great. We look forward to that.

Dr. Sharpless, your predecessor at NCI, Dr. Doug Lowy was well-known for his research on HPV and the HPV vaccine. Part of the Cancer Moon Shot isn't just the cancer research, but it is what NCI can do to help prevent cancers and protect them. Over the past few years, there has been new NCI focus on making sure that there is greater uptake of the HPV vaccine across the country.

Do you intend to continue with that? If we discovered the cure for cancer, there would be parades in the streets, but here is an actual vaccine that prevents cervical and a whole host of other cancers, I think it is important. Are you committed to continuing those initiatives?

Dr. SHARPLESS. Very much. I should mention that Dr. Lowy continues as my deputy director. He has been incredibly invaluable in that regard, because entering the Federal processes as an academic is challenging so I really appreciate Doug and his work in this area is wonderful.

Yes, we have a robust, huge portfolio in this area. I think one of the most important studies is a trial of one versus two doses of the vaccine. Right now the recommended is three doses. That is a big issue in terms of implementation in the community. So if one dose worked well, that could be game changing for subjects in the United States as well as globally with cervical cancer is a bigger problem.

Ms. CASTOR. I guess it is a good reminder, it is back to school time. This is a vaccine that is appropriate. It is important for boys and girls, middle schoolers to get the HPV vaccine to prevent cancer in the future. Is that correct?

Dr. SHARPLESS. Yes, right. A number of vaccines that prevent cancer HPV, Hepatitis B, for example, the dissemination of those things that work into the community is a real challenge for us in terms of the inflammation science to make these effective therapies more available.

Ms. CASTOR. Thank you very much. I yield back.

Mr. BURGESS. The chair thanks the gentlelady. The chair recognizes the gentleman from New Jersey, Mr. Lance 5 minutes for questions, please.

Mr. LANCE. Thank you, Mr. Chairman. Good morning to you both and thank you for your enormous public service.

For Dr. Gottlieb, the Orphan Drug Act has helped to create a market based system, to encourage the development of new medicines for people living with rare diseases, most of whom are children. As you know, I am the chair of the Rare Disease Caucus in the House.

In exchange innovators are granted 7 year monopolies in a specific disease area. Since the act was established in 1984, medicines have been brought to market for only some rare diseases, and there are many rare diseases as you both know where there are no medicines at all.

For many of these diseases, however, there has been zero second generation, newly innovative medicines brought to market for patients. In the field of Lysosomal storage disorders, for example there have been enzyme replacement therapies for eight different rare diseases. The cost on average is nearly \$500,000 per patient per year. However, with the exception of Gaucher disease, not a single second generation therapy has been approved for any of these diseases, since these first generation ERT approvals, and most of those approvals date back at least a decade.

In your view, Dr. Gottlieb, have we created perpetual monopolies in many rare diseases, especially in the areas I have discussed? And what are the barriers to moving innovation forward to spur competition and innovation and to bring newer, better medicines to patients with rare diseases as rapidly as possible?

Dr. GOTTLIEB. Thank you for the question, Congressman. I think this cuts to some of the other issues we discussed here today so it is a very relevant question.

I do believe that there are settings where it is harder to bring second to market competition into certain categories. I would argue this is one of them. It is particularly the case when you have drugs that target degenerative diseases, significant unmet medical needs, small populations. It is hard to run clinical trials with new drugs once one therapy is available. Typically, the subsequent drugs will have to be studied on top of the available therapy and you will have to show improved efficacy, with combination therapy, as opposed to just monotherapy. It is hard to run head-to-head comparative studies when already effective therapy is available. People don't want to forego an effective treatment, especially when you are dealing with a child with a degenerative disease.

I think there are a lot of things we can do. Earlier this year we published it in conjunction with our counterparts in Europe, our regulatory counterparts in Europe, a master protocol, if you will, for Gaucher's disease and how you can study multiple drugs within the context of the same clinical trial. Structure for Gaucher's, we have talked earlier about trying to develop natural history models to model. The behavior of patients who go untreated. We know how these diseases progress.

We know how they affect patients. We should have really robust natural history models to model be able to model that affect so we don't have to enroll patients on placebo trials. It relies much on placebo and that would make trials easier to conduct.

So there is a whole host of clinical trial reforms that I think we can pursue to try to facilitate second to market innovation, which I agree with you is critical in these areas.

Mr. LANCE. Is there something more we should be doing statutorily here in the legislative branch of government, Doctor?

Dr. GOTTLIEB. I would be happy to have that discussion with you. I think there is a lot of things that we can do, that we are trying to do, and will do. I think one thing that I would just affirm—and I had this discussion with the chairman about the natural history models—we allocated \$6 million earlier this year to develop six natural history models, Myotonic dystrophy 1, a natural history model for the affects of sickle cell disease on the kidney, but we did in our budget this year request additional funds to develop up to an additional 20 natural history models, and those would be focused on these diseases areas, these very orphaned, if you will, super orphaned diseases we would focus on the resources there.

Mr. LANCE. Thank you, I look forward to working with you as we have in the past. I have been the chair of the Rare Disease Caucus for quite some time. And this is completely bipartisan in nature. And we look forward to continuing the discussion. Dr. Collins, it is always a pleasure to see you.

I note in the audience John Crowley who has been very much involved in the rare disease space and his daughter Megan, and they are residents of New Jersey. And there is no one who is fighting for progress in the rare disease space more than my friend Mr. Crowley.

Thank you, Mr. Chairman. I yield back the balance of my time.

Mr. BURGESS. The chair thanks the gentleman. The gentleman yields back. The chair recognizes the gentleman from Virginia, Mr. Griffith, 5 minutes for questions, please.

Mr. GRIFFITH. Thank you very much, Mr. Chairman. I do appreciate it. I appreciate you all being here today.

On June 8, 2018, Dr. Gottlieb, the committee sent FDA bipartisan oversight requests for information about the FDA increasing criminal enforcement at ports of entry to combat the opioid epidemic, an initiative that you have championed and we support. The letter has only six requests, some of the requests were first posed by an email to the FDA Office of Legislation on January 30th of year. It is now late July and the FDA continues to tell the committee staff of letters in clearance.

Commissioner, could you help expedite the clearance of this letter so the committee has the FDA's response before the end of July?

Dr. GOTTLIEB. I absolutely will. It is in clearance. And we in an effort to try to improve transparency and get the information out publicly, I did make a lot of the information, if not most of the information that is going to be in that letter, available publicly in some remarks I gave at a forum we had to try to work with internet stakeholders to address opioid sales online. So I have made the information public. I can make those remarks available to you. I think we have made them widely available. But I recognize the importance of getting the formal response back to Congress and I am on it. I have some of my own challenges up my line.

Mr. GRIFFITH. I appreciate it. Well, and you have so much to do and I really thank you for the good work that you are doing. And there is a lot of different areas that we have been working on together.

Dr. GOTTLIEB. Thank you.

Mr. GRIFFITH. And I appreciate that very much.

What further improvements will FDA make to the expanded access program to ensure the process is effective and efficient for providers and patients, particularly now that the Federal rights to trial legislation has passed? And while I like the House version better than the Senate version, we have got the Senate version. Give me an update on that.

Dr. GOTTLIEB. Well, we have a process underway right now, a working group that is looking at what steps, if any, we ought to take to facilitate the proper implementation of the right to try measure. It is going to be a pathway that sits alongside our extended access program. We are still going to operate our extended access program.

We did bring in an outside group, an expert group to take a top down look at our expanded access program and make some recommendations to the agency on how we can improve it. I am going to make that public soon to provide some transparency around what they found.

But we think that there are additional process steps that we can take to make it easier for people who aren't as sophisticated or physicians who haven't done this before to access that. We are also working with Friends of Cancer Research and the Reagan-Udall Foundation to create a platform to have sort of a one site of entry, if you will, to get information about what expanded access programs exist.

I think the challenge still remains that the difficulty, sometimes reluctance, but a lot of times difficulty of sponsors to actually make drugs available especially when we are dealing with things like some of these cell based therapies or biologics cost aren't trivial, when you are a small company you barely have enough product for the clinical trials. And I have been on the other side of this, so I know how that is. And so I think we still need to look for ways to provide proper incentives to try to make sure that when we have really really promising therapies we might be able to have supply available too to make that available to patients.

Mr. GRIFFITH. Well I appreciate that. I have been an active proponent for right to try for many years. And if people are facing death, they will take that Hail Mary pass and take whatever they need to, if they can. Let us know what we can do to assist you on that as well.

Dr. Collins, I am going to ask you a couple of questions just to give me update. I have a partial answer that I already found on the internet and that is with Lou Gehrig's ALS, I understand you all had a breakthrough this spring. But I also am interested in Huntington's chorea, and I obviously ask about these because I have friends who have been afflicted with both of those.

Dr. COLLINS. Those are both terribly important and often tragic neurological diseases that result in neurodegeneration. With ALS, as you mentioned, there has been encouraging development of a new therapeutic approach this spring still very much in the process of being evaluated.

Huntington's disease I will actually reflect a bit on, this was 25 years ago that my own laboratory was involved in the discovery of gene that is responsible for that condition. And it has been very gratifying to see in the course of just the last year or two, a still and a mouse model, very encouraging information about using a genetic approach to try to block the production of the toxic protein.

And now in human clinical trial, which we are waiting for the full data to be rolled out, but sounding encouraging, a similar possibility that utilizing a molecular therapy injected into spinal fluid, which then gets into the brain, may very well be able to provide benefit.

And goodness knows, we have waited a long time for that kind of thing to happen. So it is pretty exciting to see. We have a long way to go I think before we can say really have the answers, but this is a lot different than saying we have nothing to offer.

Mr. GRIFFITH. I appreciate that very much and yield back.

Thank you, Mr. Chairman.

Mr. BURGESS. The chair thanks the gentleman, the gentleman yields back. The chair recognizes the gentleman from California, Mr. Cárdenas, for 5 minutes for questions please.

Mr. CÁRDENAS. Thank you very much, Mr. Chairman and ranking member. I appreciate the opportunity to openly discuss with the witnesses the progress that we have made. And not every day do we as United States Congress actually pass laws that we can actually look at and say, I think we did something good. And so I want to thank all of the implementers for doing good work.

My first question has to do with the diversity in research of subjects. So thank you for testifying today. I was excited to read in

your testimony, Dr. Collins, that about 85,000 individuals have already started the enrollment process for the All of Us Research Program; “70 to 75 percent are from communities who have been historically unrepresented in biomedical research and almost 50 percent are specifically from racial and ethnic groups who have not been included in previous research.”

As you all know, diversity in medical research has long been an issue. I believe one way to decrease health disparities in this country is to ensure that we are including individuals of all races and ethnicities in medical research.

So with that, my question is what is NIH doing to ensure that All of Us research program recruits a diverse group of participants that is racially and ethnically diverse?

Dr. COLLINS. Well we track that week by week. I personally am asking for that information every week to see how the enrollment is going. But I am going to ask Dr. Duvaney to say how this is being done because this is unprecedented to have this level of diversity.

Ms. DEVANEY. Yes. And thank you for the question. This is perhaps our strongest priority as a program, understanding that ultimately a lot of the data scientists are using today is not reflective of the diversity of the country and that what we are learning is not applicable to all communities.

We have a number of different ways in which we are attempting to reach out to diverse communities. And just go into it with the understanding that we are going to try things, and it is not going to work, and we are going to go have to shift and try new things.

One of the things I would just like to highlight is working with community partners. We have a number of community engagement partners across the country who are helping us to build trusted relationships with their communities at a local level. And our chief engagement officer, Dr. Dara Richardson-Heron at the NIH has been really working with those groups in a very robust way. And beyond our first foreign inaugural partners we have about 30 plus partners that are national that are helping us to build awareness within our communities.

Mr. CÁRDENAS. So you are talking about groups that are more local and actually might have a propensity for working with a particular population, whether it is an immigrant population, or a Hispanic population, or a Black population, et cetera. So working with local groups who already have relationships with those communities?

Ms. DEVANEY. That is right, exactly. Yes.

Dr. COLLINS. When we did the launch on May 6 in seven different places I was in New York at the Abyssinian Baptist Church with an African-American community that was totally revved up about the opportunity to be included this time.

And I have to give credit to 21st Century Cures about this focus on inclusion. You have given us some additional tools there in many different projects across the board, but All of Us is really turning out to be a flagship here about how to do this in the most visionary way.

Mr. CÁRDENAS. OK. So this opportunity for us to remind ourselves that diversity and research when it comes to subjects in par-

ticular communities, et cetera, because we all genetically have different reactions, et cetera, and different propensities when it comes to certain diseases and cause and effect, correct?

Dr. COLLINS. Absolutely. And one should not assume that when you see a health disparity that that is something that is readily understandable on the basis of looking at one thing. Usually these are a combination of environmental exposures, of stress levels, of some genetics in there. But one shouldn't overinterpret that part because we are awfully similar at the DNA level. And if you really want to understand the health disparities, you need to have these comprehensive studies that collect data from all those perspectives and then figure out how to intervene.

Mr. CÁRDENAS. So it is better to have good research rather than having to force yourself to extrapolate out, and then that is more guesswork and that is not necessarily scientific.

Dr. COLLINS. You want to have the data on the people for whom you are going to then offer some answers. We just heard from Dr. Sharpless a few moments ago about this big study they are just starting with African-American prostate cancer. Another example, where we don't understand, why men who have prostate cancer, who are Black, have a higher likelihood of dying and a higher likelihood of aggressive disease. We need to know that.

Mr. CÁRDENAS. OK. So what are some of the challenges associated with building a cohort that is racially and ethnically diverse? Do we have some findings or things that we are hoping to tackle in the near future that maybe you learn by venturing further into this diversity effort than ever before?

Ms. DEVANEY. Yes. Well, we are just at the beginning of this journey. So we would love to follow up with your office and talk about this more. I will say we have community advocacy groups and participant advisory boards, at all of the health care organizations that are part of our program that are helping us understand what is working, and what is not working, messaging what is not working as part of—even things like your parking isn't close enough to the clinic, and therefore it is too hard for me to make the appointment time to come in and donate my samples. So we have been learning a lot just from participant feedback and would be happy to share as we learn more.

Mr. CÁRDENAS. So as an engineer myself, having a good feedback system and adjusting all the way is important so you are doing that.

Ms. DEVANEY. Yes.

Mr. CÁRDENAS. OK. Thank you very much Mr. Chairman and thank you for the generosity of time.

Mr. BURGESS. The gentleman yields back. The chair recognizes the gentleman from Missouri, Billy Long, for 5 minutes for questions, please.

Mr. LONG. Thank you, Mr. Chairman.

And I would like to get one more shout out to Diana DeGette. Diana is my co-chair on a congressional study group on Japan. We travel to Japan together every year. And also to Fred Upton for their tireless work on this 21st Century Cures and they just did yeoman's work as a lot of you know. So I want to give one more shout out to them.

My youngest daughter when she was 25 years old diagnosed with Hodgkin's lymphoma. Today she is 29 years old, she is 3 years past chemo. So the developments over the years as Dr. Collins was talking earlier have been phenomenal. And I want to thank everyone.

Dr. Sharpless, we were happy to support the Cancer Moon Shot funding in the 21st Century Cures and are looking forward to hearing about progress for patients. Can you tell us about the most exciting thing that is being supported in the Cancer Moon Shot?

Dr. SHARPLESS. Well, that is really tough. There is so much good stuff. I think this is a very meaningful law for patients with cancer. And I think it is impacting in many ways. We already talked about the response studies, maybe I will talk about the rare tumor initiative, which is also a very exciting initiative. We mention rare diseases, many rare cancers actually are hard to study for some of the reasons that came up. They are rare, they are hard to do clinical trials.

And the NCI is a good place to study those things. We can have patients with a certain rare disease come to the NCI and get their care here. And this paradigm works and the Moon Shot trying to build on that experience. So for example, in the area of a disease called RASopathies where different mutations that activate RAS, a driver protein in cancer, those patients generally present with childhood tumors.

And the NCI now has a recent trial that we just had presented at ASCO shown here on the left is a slide of Andrea Gross showing, one of our scientists—showing results of selumetinib trial in this RASopathy patients.

So this is a patient with NF1 deficiency. And my executive summary was the tumors shrink, the kids feel better and the drugs seem safe. Yay. And then a few parents contacted me and said, my child was on this trial, actually and the responses have been marvelous.

And so shown is the picture of the child pretreatment on the left. This is Phillip after treatment. And you can see his windpipe, his airway is not being compressed by the tumor anymore, and he has not the social stress of going to school with a big lesion like that. So this is a sort of a precancer syndrome. This is mutation that activates RAS, this cancer gene. And this kind of study is a really great thing for the NCI to take on because of our integral program.

Mr. LONG. OK. And in the testimony it says we must transform the way we conduct research, the way we share results, and the way we get discoveries into patient's care. Could you discuss how NIH is helping transform infrastructures needed to help meet these goals?

Dr. SHARPLESS. For junior scientist you mean?

Mr. LONG. Yes.

Dr. SHARPLESS. Yes. Yes. So the new funding from Congress has made it possible to increase the success rates for new scientists applying for their first grants, so it is called R01 grant. So in NCI for example has set aside enough funds to increase that amount by 25 percent. We similarly are trying to link in the period of the award. We think that that will allow the scientists to concentrate on their science and not much bureaucracy in terms of writing grants.

So we are testing out a 7-year award as opposed to a 5-year award. And one of the things we are really doing is thinking about the training opportunities we are providing for young scientists, both in the postdoctoral setting and in the faculty setting, to make sure they get the right skills, for example in big data, which is something that we really need more training for.

Dr. COLLINS. If I may, just across all of NIH, and again thanks to the 21st Century Cures and Next Generation researcher initiative, which is part of this bill, we have put into place efforts to provide a better chance for early stage investigators coming to NIH with their first major grant application to get funded, and then to have sustainable support so they know they have a career.

This year, fiscal year 2018, we are predicting we will fund the largest number of first time investigators ever at NIH because we have made this shift in priorities and you helped us with that, with 21st Century Cures.

Mr. LONG. Thank you. I had a chance to meet with two early career scientists from the American Association of Cancer Research. And I was very impressed with the excitement and passion they have for careers in cancer research and helping cancer patients. And once again as a father of a cancer patient survivor it really means a lot to me.

Thank you all for being here, and thank you for being here today, you all too.

So I yield back.

Mr. BURGESS. The chair thanks the gentleman. The gentleman yields back. The chair now recognizes the gentleman from Maryland, Mr. Sarbanes, for 5 minutes of questions, please.

Mr. SARBANES. Thank you, Mr. Chairman. Thank you all for coming today. Whenever you testify I am reminded of the tremendous responsibility that you have heading the organizations that you do. And I am going to thank you for your work to implement 21st Century Cures, which obviously as you know is a point of real pride for this committee. So thank you for that.

Commissioner Gottlieb, I wanted to ask, I know there have been some discussions already about the biosimilars action plans that you released. I commend you for that. I have just introduced in the last few days something we are calling the biosimilars competition act, which is try to get to some of these pay for delay agreements that are operating in the biologic, biosimilar space in the same way that we have given authority to the FTC to kind of police that conduct with respect to brand name drugs and in generics where it has been consequential for sure. That the authority is there, that they can look at these agreements, they can judge whether they are fair and appropriate, vis a vis the consumer or not—there are tremendous savings to be had there.

I think maybe the figure is that brand names occupy about 20 percent of the drugs that are produced every year, but it is still 75 percent of the cost that is out there. And I think that includes the sort of biologics, biosimilar distinction as well. Can you just speak to anything that is a good idea for the FTC to have this authority?

And also, I think you understand from the plan that you put forward in your comments generally that you look for ways to cooperate with an agency like the FTC around this kind of thing to make

sure that we are getting these drugs at the price point that they should be at.

Dr. GOTTLIEB. I thank you for the question, Congressman. I haven't looked specifically at the measure, but I will. It is a little bit outside the scope of my authorities. I have my own equities with FTC in trying to work with them to try to see how we can facilitate their interests and potentially bring in cases related to delaying tactics it might involve for example the REMS where we can help provide information that could prompt them to take a look at whether those practices are anticompetitive and that has been a big bugaboo of mine as well.

Generally speaking, we like to approve safety biosimilars and we like to see them marketed and we like to see patients benefiting from them.

So culturally we like to see drugs marketed. It is the fact that most of the biosimilars that have been approved have not been marketed for various reasons. The biggest reason is in patent delays. It is also a fact that a growing number of small molecule generic drugs end as being approved but the drugs are never being marketed because of the changing economic dynamic to that market as well as. And I think we need to keep a close eye on that as well, because competition may be declining in the small molecule generic world as well.

Mr. SARBANES. Thank you. And we will try to get this tool into the toolkit that the government has broadly to make sure that we are protecting consumers in that space.

Let me switch gears real quick. To you, Dr. Collins. And I know you got a question earlier I believe about Alzheimer's research generally and some of the clinical trials associated therewith. But there was an article in The New York Times yesterday that pointed specifically to the challenge that is presented by trying to find sufficient people to participate in these trials.

There are a lot of trials that are underway or are on deck that would suggest the need for up to 25,000 participants in these trials. And some of them could be really breakthrough, but I gather that this is a real problem, challenge, trying to find enough participants.

Can you speak to what you know about that and what can be done about it?

Dr. COLLINS. Yes, thank you. That was based upon comments made by Dr. Marie Bernard who is the deputy director on the National Institute on Aging at the major Alzheimer's meeting that was held in Chicago.

This is a challenge because we are now at the point where we are trying to recruit individuals who don't yet have cognitive decline, but who are at high risk for Alzheimer's by increasingly accurate means that we have, some of them using imaging, some using genetics, and we need a lot of participants in order to do that. But now we are reaching out to people who may not be that motivated to take part in research because they are fine, right now.

We are arguing that that is the best time to intervene, but it is not so easy to enroll. I will say one of dreams I have of the All of Us program that we have been talking about there program where you have a million participants who are preconsented for recontact for reach protocols that that would be a fantastic group to be able

to enroll participants in studies like this for common disease, whether it is diabetes, or hypertension, or Alzheimer's.

But right at the moment where we don't have that platform, we really have a challenge trying to convince people that this is going to be something they want to take part in. We are pulling out all the stops. And again the Congress having made Alzheimer's such a high priority for us. We have resources in order to do that kind of recruitment, but it is not simple because it is a different model than what people are used to where you get approached about a clinical trial when you already have the diagnosis. Here we are approaching people who don't have that diagnosis trying to figure out how to prevent it.

Mr. SARBANES. Thank you very much. I yield back.

Mr. BURGESS. The chair thanks the gentleman. The gentleman yields back. The chair recognizes the gentleman from Indiana, Dr. Buschon, for 5 minutes of questions, please.

Mr. BUSCHON. Thank you, Mr. Chairman. Thank you all for being here. Honestly it is pleasure for me to be here. As a physician, I never thought I would get to talk to you all. And I was at an event with Dr. Sharpless with Steve Rosenberg and Diana DeGette recently. And the work that he has done over the years. I can't even express how much of an impact he has had.

Dr. Collins, you just said high risk. Who is high risk for Alzheimer's?

Dr. COLLINS. Well, anyone who gets to be 85 or 90 is at high risk.

Mr. BUSCHON. No, I am saying that people who don't know they have it, if your mom has it, your dad has it, your grandma? Maybe if one of your family members has it, you are high risk. I don't know.

Dr. COLLINS. So there are there ways in which we are currently identifying such folks. One is we that you have a very strong family history, almost inherited in a dominant fashion. In fact, it is a dominant fashion. And there are those families that if you are in one of those circumstances we can track the gene in the family and figure out who has it long before any symptoms.

Another way is to look at a genetic risk factor called ApoE4. If you have one copy of that, your risk goes up threefold. If you have two copies, one from each parent, it goes up 15 fold so those people are very high risk. And the third way is scanning using a PET scan that picks up amyloid, because amyloid starts depositing in your brain probably 20 years before the first cognitive decline symptoms. So if people who are worried about this are willing to do a scan, we may be able to say, hey, you are one of those that ought to get into this clinical trial.

Mr. BUSCHON. So if somebody out there is watching C-SPAN right now and they are sitting there going, hmm, I wonder if I am high risk. I understand the technical tests and things that you do, but people need to say well, my mom had it so I am high risk. You know what I am saying?

Dr. COLLINS. And indeed that is one.

Mr. BUSCHON. That is one of them, right?

Dr. COLLINS. There are other ways to try to be more precise about it. If people are watching C-SPAN out there and are wondering hey should I take part in this? We just heard how difficult

it has been sometimes to get the word out there. The place to go is clinicaltrials.gov which posts the trials on Alzheimer's disease and everything else where you can find out who is doing a trial, what are the enrollment criteria, who do you contact to learn more about it? All of this we do very closely with the FDA as a partner.

Mr. BUSCHON. Great, thank you.

Dr. Gottlieb, my wife's an anesthesiologist she is out in the field today practicing medicine. She just texted me. She didn't even know you guys were here. And she says, hey, can you check into the fentanyl shortage, because—no, I am not kidding she just texted me.

Mr. LONG. She is watching C-SPAN.

Mr. BUSCHON. No, she doesn't. She is actually practicing medicine. And we have demonized Fentanyl, the illicit forms of Fentanyl, but this is a very, very common anesthetic agent. And apparently there is going to be a long term back order on Fentanyl. Which is honestly going to be a huge problem.

You don't need to answer the question, I just want to point out that what you are doing on drug shortages has real everyday, and you know this, but for everyone else out there, clinical implications in the practice of medicine. She says Zofran, other common paralytic agents that she uses daily in her anesthesia practice are really in short supply. Fentanyl is a new one on me though, she just texted me that.

So thank you for work on that and your response earlier on what you all are doing on that. If you have any other further comments. Because I have one other question for you.

Mr. GOTTLIEB. I will just say these are structural problems, as I mentioned before, and whatever is in shortage say 6 months from now I guarantee it is going to be something different. I have grappled personally with these as well, as a hospital based physician, so this impacts patient care. We are working very hard on this.

Mr. BUSCHON. I know you are. So 21st Century Cures sought to implement personalized medicine and seek cures. This is a little proprietary question here, for diseases such as cancer which rely on diagnostics, and I know your staff probably has told you I might ask about this, unfortunately the current diagnostic frameworks for laboratory developed tests, LDTs in vitro diagnostic test kits haven't been updated since 1988, 1976, and 1988. That is why Diana DeGette and I and other members of the committee have released the Diagnostic Accuracy and Innovation Act, DAIA, so to speak, to update how diagnostics are regulated.

We have had a discussion draft out there for a long time you all have had that and we really appreciate your input. And we have talked to laboratories, patient groups providers and others and we really need reform now.

And so I know you are familiar with the issue and I brought it in the past, as well as the committee's last hearing. You recently gave us a narrative on what the FDA provided us earlier this year in response to DAIA, but I want to get diagnostic reform done this Congress hopefully.

So we are waiting for the red line of the bill from FDA and I wanted to know if you have any insight in that progress?

Dr. GOTTLIEB. It is very close, Congressman. We have completed most of our work and I hope to have it to you very soon. I would be happy to come into your office and brief you on it as well, but I think we are very close.

Mr. BUSCHON. Great. I just want to reiterate you have been very helpful and I am very appreciative of that. And we are hopeful to get this accomplished this Congress.

Thank you, Mr. Chairman. I yield back.

Mr. BURGESS. The chair thanks the gentleman. The gentleman yields back. The chair recognizes the gentlelady from Indiana, Ms. Brooks, 5 minutes for questions, please.

Mrs. BROOKS. Thank you, Mr. Chairman and thank you all for your service to our country and for all of the incredible medical innovation. I just want to thank you, because you all could probably be doing very, very different things in our country and yet you are here, working on behalf of all citizens, not just here but actually around the globe.

Dr. COLLINS. I would like to ask in your testimony you mention that there are provisions that provide direction from Congress to ensure specific subgroups of patients are specifically included in research in clinical trials. I am particularly interested in childhood disease and cancers.

And having heard from constituents who have lost a child to cancer and are currently fighting the disease, we know that NIH is focused on improvements for children. That is an area that has been lacking in the past. Can you elaborate on the implementation of the recently passed Childhood Cancer STAR Act, which was signed into law in June and what kind of innovation are we focused on for childhood cancers and disease?

Dr. COLLINS. I ask Dr. Sharpless to respond to that.

Dr. SHARPLESS. I thank you for the question on childhood cancer. It is important to say two things about childhood cancer. While it is true we have made tremendous progress, fewer children are dying of cancer than ever, we are still having, also true, too many children die of cancer.

And in particular, even when we are able to cure kids of cancer, we often leave them with lifelong toxicity, so they have survivorship issues. And I think that is one of the principal issues the STAR Act tried to address is the issues of novel therapies for kids with cancer, and then also, the burden of survivorship that some of these patients incur through their curative therapy.

And so the NCI is really interested in this topic. This was a personal research interest of mine when I was in academics, so I know firsthand the pain that many of these patients go through or the suffering that this entails.

And I think we have a focus on new research efforts related to survivorship, biospecimen acquisition, and then getting new advice and new voices into the NCI, to make sure that we are adequately advised from the expert community on pressing issues in survivorship.

So thank you for the leadership on that important act.

Mrs. BROOKS. Thank you very much.

Dr. Gottlieb, as my colleague, Anna Eshoo, talked about, in our focus on PAHPA reauthorization, which it is critically important we

get that reauthorized by the end of September, one of the things that has come up in various discussions with Dr. Kadlec and others is the importance of platform technology, the use of platform technology when it comes to innovation with vaccine.

Can you talk about that to some extent, because there has been frustration on this committee about egg-based vaccines versus platform technology? Or if anyone would like to comment. I am starting with you, but—

Dr. GOTTLIEB. I would like to start, if I can. I appreciate the question very much. And we have a proposal in the President's budget for some additional funding for the agency to try to support continuous manufacturing, alternative manufacturing. And we think this is really the direction that we want to head in, where you have closed, continuous manufacturing platforms, particularly with recombinant technologies, where you can effectively have, like, cassettes that you basically plug into the platform and can allow continuous manufacturing of a vaccine.

And if you want to modify the vaccine, you can literally plug in another cassette that codes for a different permutation of the same vaccine, same recombinant vaccine.

We think that this is really the solution or a solution for influenza seasonal flu, the ability to scale up manufacturing more quickly and produce vaccines closer to the flu season so you can guess the strain better as well as have a platform available in the event of a pandemic flu. And these same technologies can be used to try to scale up manufacturing of other vaccines.

In an ideal circumstance, what we would have isn't mothballed vaccine that degrades over time if it is not stored correctly and takes up a lot of space and is costly, but platforms that allow quick manufacturing of vaccines should we need it.

Mrs. BROOKS. I am assuming, Dr. Collins.

Dr. COLLINS. NIH works very closely with FDA in this space. If Tony Fauci was here, he would go into this in some detail, that the idea of having to build things in eggs is so much yesterday's technology.

And the concrete example this past year, with the flu vaccine having been surprisingly ineffective. It turns out that the virus mutated in the process of being grown in the eggs; and so, therefore, it turned out not to be a particularly effective vaccine for something that we didn't have control over.

These new platforms, which allow you to build vaccines in a much more rapid fashion, and much more directed fashion, DNA-based vaccines, RNA-based vaccines. Once you have that platform going, you can, very quickly, adapt it to many different pathogens. And that is certainly something we are working on now, to develop this universal influenza vaccine, which is a very high priority, and Congress has given us some additional funds for that, so that we wouldn't have to have the yearly effort to try to guess right. You would have a vaccine that works against virtually all strains and would also be effective against that next 1918-style pandemic, which we are all worried about and which is overdue.

Mrs. BROOKS. Thank you. And we did include a Pan Flu provision in the PAHPA legislation passed out of this committee.

With that, I yield back. Thank you for your work.

Dr. COLLINS. Thank you for that.

Mr. BURGESS. The chair thanks the gentlelady. The gentlelady yields back.

The chair recognizes the gentleman from Florida, Mr. Bilirakis, 5 minutes for questions.

Mr. BILIRAKIS. Thank you, Mr. Chairman. I appreciate it. And I thank the panel for their testimony today as well.

Well, the first question I wanted to ask is, we talked about Alzheimer's disease, of course, and what about Parkinson's? We are talking maybe how do you know if you are a candidate for Parkinson's disease to participate in these clinical trials, if there are no symptoms? It may be in the early stages. And if you could answer that question, sir, I would appreciate it.

Dr. COLLINS. There are parallels here that are notable. There are genetic risk factors for Parkinson's disease, which is interesting, because when I was in training and I asked my professor, "Are there any diseases that don't have genetic contributions?" And he said, "Oh yes, everybody knows Parkinson's is always totally random and sporadic." Well, he was really wrong.

So if you have a variant, for instance, in a gene called LRRK2, your risk of Parkinson's goes up. If you have a variant in a gene alpha-synuclein, your risk goes up. We are beginning to, therefore, be able to identify people at high risk and invite them to take part in prevention trials.

Another big thing that has happened in Parkinson's disease in just the last 6 months is the formation of a partnership with industry called the Accelerating Medicines Partnership for Parkinson's Disease with FDA as a critical partner in this as well, and really, now, figuring out how we could learn from a very large amount of data that is out there, but hadn't been brought together, what are the next generation of drug targets for Parkinson's disease and how do we accelerate the process of getting there? Because we have treatments, L-dopa has been around a long time, but we certainly don't have things that actually prevent progression. They more treat the symptoms. And we believe we could do better with that.

I should also say the BRAIN Initiative, which is this very bold effort supported by 21st Century Cures and the Innovation Fund, is learning things about the wiring diagram of the brain that is going to be very relevant to some of the things that are being done for Parkinson's disease, with direct brain stimulation, where you actually put an electrode into the brain to try to take care of some of the motor problems. What we do right now is kind of clunky. As we learn the wiring diagram, we could be much more precise and effective about that.

Mr. BILIRAKIS. Well, thank you very much. Anyone else want to add something with regard to that? OK. Thank you.

Dr. Gottlieb, Section 3088 clarifies that FDA has the authority to grant emergency use authorization for animal drugs, allowing the agency to approve the GMO mosquitoes for, again, Florida's Zika problem. We are planning ahead.

Would you provide an update on the implementation of Section 3088, specifically as it relates to approval of the GMO mosquitoes?

Dr. GOTTLIEB. I can get back to you with a more detailed update on that, Congressman. But I will tell you, there has been some dis-

cussion about the nexus of authority with EPA for some of these products. But we did provide a guidance earlier this year, I believe, that addressed some of these issues. So I can get back to you with more specifics about where that stands.

Mr. BILIRAKIS. I appreciate that very much.

Dr. Gottlieb, a second question: As a long-time champion and supporter of policies that seek to promote a deeper level of patient engagement in the therapy development processes, I am pleased with the progress the agency has made under your leadership—so congratulations, and we appreciate all you do—including the FDA’s moving ahead to implement the Patient-Focused Impact Assessment Act provision of Cures that requires the FDA to disclose how patient engagement data informed a review of any approved product.

Where is the agency presently in implementing this provision, particularly efforts to standardize the inclusion of such information in the record of approved drugs so that it is accessible and understandable?

Dr. GOTTLIEB. We have issued one of four guidances that we intend to relay to patient-focused drug development, and we have standardized a format for the presentation of patient-related information in clinical trials.

So when a clinical trial is submitted to us, there is a discrete, a very explicit section for patient-focused information. And on the medical device side of our house, we have done some similar things: We are seeing a very high rate of the use of patient-focused information, and PROs, in the development of medical devices as well. So this is a cross-agency effort across all of our Medical Product Centers. We also just stood up a Patient Affairs Office inside the Office of the Commissioner reporting in to the principal deputy that is going to help advance some of these policies, really, a coordinating office to provide a focus of access for patient groups, but also, a focus of policymaking when it is cross-agency policymaking around these issues.

Mr. BILIRAKIS. OK. Thank you very much.

I yield back, Mr. Chairman.

Mr. BURGESS. The chair thanks the gentleman. The gentleman yields back.

The chair recognizes the gentleman from Georgia, Mr. Carter, 5 minutes for questions, please.

Mr. CARTER. Thank you, Mr. Chairman. And thank all of you for being here and thank you for your efforts in implementing 21st Century Cures, legislation that I personally feel like is some of the best legislation we have passed in Congress in quite a while, so we are very proud of, particularly coming out of this committee.

Dr. Collins, I will start with you. I wanted to ask you particularly about one of the initiatives of 21st Century Cures, and that was to, really, review the regulations and policies with respect to research in laboratory animals. And as I understand it, you are working with USDA now and the FDA to try to complete a review of that. And I just wanted to ask you if you could tell us the current status of that review, and when do you anticipate the completion of that review?

Dr. COLLINS. I appreciate the question. We are very seriously engaged in this. And, again, 21st Century Cures gave us some clear guidance about what we ought to engage in. We did put out an RFI back in March to ask for comments in this area, in terms of whether the oversight that we currently apply to animal experimentation is sufficient or whether it has areas that are overly bureaucratic, which has been a concern.

Obviously, we are deeply concerned about maintaining our ethical responsibilities, in terms of how we take care of animals that are subjected to various experimental approaches, from which we learn a great deal that has led to many medical advances.

We got 19,000 responses to that request, and they are currently being sorted at the moment. We would expect, therefore, to have, based upon those, a draft set of recommendations about animal care and use, sometime probably in September. We will then need to have responses to that. And so we would hope to have a final version of this by December or early in 2019.

Mr. CARTER. Great, great. Any opportunities that you have identified thus far that may help you?

Dr. COLLINS. I think there are concerns that some of the requirements we put on grant applicants in terms of animal care and use could be delayed until the award is actually made as opposed to asking them to have all of those things in place when they submit an application, because that can add a lot of time and effort.

And obviously, our concern is, if we are going to actually make the award, we want to be sure that the animal care is being done in the best possible way. That is one area. Obviously, there are differences of opinion here.

Mr. CARTER. Yes.

Dr. COLLINS. And we are seeing those in those 19,000 responses. And at some point, we have to try to come down in what we think is a fair and balanced approach.

Mr. CARTER. And I am sure you will reach that. I am very confident. Let me switch gears here and talk about something that is very exciting to me as a pharmacist, and that is precision medicine. And that is something that I see in genomic testing and everything is something I see as the wave of the future, and great opportunities for us in healthcare.

But I am concerned, when we get all this data in, we are struggling already with our electronic health records. How are we going to handle this? I want to ask you that, and then I would like to ask Dr. Gottlieb as well.

Dr. COLLINS. Well, I will say a word, and then I will ask Dr. Devaney to say a little more, as the Deputy Director of the All of Us Program. We are very invested in looking at this in the fashion that is cutting-edge, as far as dealing with very large datasets, putting the data into the cloud.

We just had a very interesting all-day workshop on Monday on artificial intelligence and machine learning and how that can be applied to these unprecedented datasets to glean the maximum amount of information out of there while, at the same time, maintaining the confidentiality, the security systems that the participants in this are going to expect about their deidentified data.

But maybe, Dr. Devaney, you want to say a little more?

Mr. CARTER. Sure, please.

Ms. DEVANEY. I would love to add to that. So one of the data types that is going to be, I think, the most essential to precision medicine, or one of is information from electronic health records. And this is one of the largest challenges for our program.

We have direct partnerships with many healthcare organizations, and we are getting those data continuously from those partnerships, but we are also working on other strategies, including one in partnership with four of the largest her vendors right now, to work on making the data transmission much more seamless across provider lines and into the program when a participant authorizes it.

Mr. CARTER. Great. Dr. Gottlieb, I know this is important in drug data development as well.

Dr. GOTTLIEB. I appreciate the question. I would just take a step up the continuum to try to make effective use of the data. Because there is so much information, how can we make effective use of the data in a way that it can translate to clinical benefits to patients. And I think this is where some of the issues we talked about earlier around clinical trial innovation comes in where you have the ability now, with a seamless clinical trial design, to effectively buy us enrollment in the trial for some of the genomic information and predictive information that is likely to predict who is more likely to benefit from a treatment, and who is less likely to experience a side effect.

And so if we can use this information in that way to structure trials and enrollment, we can end up with much more information about who is likely to benefit from a drug and more tools to make sure the right drug gets to the right patient at the right time. We have talked about this for decades. We now have that technology at hand.

Mr. CARTER. And I can sense the excitement in your voice. And it is exciting for me, as a healthcare professional as well. I just look into the future of this and just think, Wow, what we have got to look forward to. Thank you.

And I yield back.

Mr. BURGESS. The chair thanks the gentleman. The gentleman yields back.

The chair needs to state that, without objection, all members' opening statements will be made part of the record.

The chair asks if the gentleman from Texas has a unanimous consent request concerning Alzheimer's. Were you going to ask that additional information be forwarded to the committee about Alzheimer's?

Mr. GREEN. If you could just send it to the committee on some of the information you couldn't have given us today because of the time limits.

Dr. COLLINS. Happy to do that.

Mr. GREEN. Thank you. I forgot what I was going to ask.

Mr. BURGESS. And also, the chair would like to make the observation that, Dr. Collins, you started out this hearing with the remark about the immunotherapy and some of the dramatic things that have occurred. And it predated our work, our passage of the Cures bill, but a former President of the United States, in July of

2015, went public with the information that he had metastatic melanoma to the brain and the liver. And remembering my time in medical school, my initial thought was, we will not have this individual with us by Labor Day. But it has really been dramatic to see him a year later deliver a speech at the Democratic Convention. A year and a half, then he was present at the inauguration in January 2017. I don't know what his clinical status is now, but it was truly dramatic.

And, again, all of you are to be congratulated for making that possible. And hats off to former President Carter for going public with the information and entering a clinical trial, because that is the way information is gathered and learned. So, again, I felt obligated to make mention of that milestone.

Seeing that there are no further members wishing to ask questions, I do want to thank our witnesses for being here today. Pursuant to committee rules, I remind members they have 10 business days to submit additional questions for the record. I ask the witnesses to submit their responses in receipt of those questions.

Without objection, the subcommittee is adjourned.

[Whereupon, at 11:17 a.m., the subcommittee was adjourned.]

