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IMPLEMENTING THE 21ST CENTURY CURES ACT:

AN UPDATE FROM FDA AND NIH

THURSDAY, NOVEMBER 30, 2017

House of Representatives,

Subcommittee on Health,

Committee on Energy and Commerce,

Washington, D.C.

The subcommittee met, pursuant to call, at 10:03 a.m., in Room 2123, Rayburn House Office Building, Hon. Michael Burgess, M.D. [chairman of the subcommittee] presiding.

Present: Representatives Burgess, Guthrie, Upton, Shimkus, Blackburn, Lance, Griffith, Bilirakis, Long, Bucshon, Brooks, Mullin, Hudson, Collins, Carter, Walden (ex officio), Green, Engel, Schakowsky, Matsui, Castor, Sarbanes, Lujan, Schrader, Cardenas, Eshoo, DeGette, and Pallone (ex officio).

Staff Present: Ray Baum, Staff Director; Karen Christian, General Counsel; Kelly Collins, Staff Assistant; Zachary Dareshori, Legislative Clerk, Health; Paul Edattel, Chief

Counsel, Health; Adam Fromm, Director of Outreach and Coalitions; Caleb Graff, Professional Staff Member, Health; Jay Gulshen, Legislative Associate, Health; Ed Kim, Policy Coordinator, Health; Bijan Koohmaraie, Counsel, Digital Commerce and Consumer Protection; Katie McKeogh, Press Assistant; Alex Miller, Video Production Aide and Press Assistant; Mark Ratner, Policy Coordinator; Kristen Shatynski, Professional Staff Member, Health; Jennifer Sherman, Press Secretary; Danielle Steele, Counsel, Health; Hamlin Wade, Special Advisor, External Affairs; Greg Zerzan, Counsel, Digital Commerce and Consumer Protection; Jeff Carroll, Minority Staff Director; Waverly Gordon, Minority Health Counsel; Tiffany Guarascio, Minority Deputy Staff Director and Chief Health Advisor; Jessica Martinez, Minority Outreach and Member Services Coordinator; Samantha Satchell, Minority Policy Analyst; Kimberlee Trzeciak, Minority Senior Health Policy Advisor; and C.J. Young, Minority Press Secretary.

Mr. Burgess. The subcommittee will now come to order.

The chair will recognize himself for 5 minutes for the purpose of an opening statement.

The 21st Century Cures Act was a monumental achievement. Cures was the product of a bipartisan, multiyear effort by the Energy and Commerce Committee that brought our laws into a modern era of medicine.

It has been nearly 1 year since Cures was signed into law. I remember remarking at that press conference a year ago to imagine a world in which government was not an obstacle but an ally in helping us deliver drugs and devices to patients and cures to patients.

Today's hearing marks the Health Subcommittee's first look into the implementation of what many in the healthcare community called a transformational bill that would positively impact not only the researchers and the scientists who are developing the latest breakthrough therapies, but physicians seeking treatment for their patients, giving hope to them, their loved ones, and their advocates.

This morning we will hear from two leaders responsible for implementing the drug development and biomedical research provisions included in Cures. I want to welcome Dr. Francis Collins, the Director of National Institutes of Health, and Dr. Scott Gottlieb, Commissioner of the Food and Drug Administration, both back to this subcommittee.

All of us know the demands your schedules put on both of you, and we appreciate you coming before us today.

At the time of the Energy and Commerce Committee's launch of the 21st Century Cures initiative, the statement was made repeatedly that there were 500 cures and treatments to address 10,000 known diseases. More progress was needed to alleviate the agony of an incurable disease.

While the United States was maintained its global leadership in biomedical innovation, there existed a potential bridge in the growing divide between the revolutionary advances in science and technology and a less-than-adequate system for discovering, developing, and delivering new therapies.

Members of the committee, both this committee and the Senate HELP Committee, held numerous public hearings, forums, roundtables in Washington, D.C., and around the country bringing together leading scientists and medical experts, patient and disease group advocates, and researchers across multiple sectors. The primary objective of these events was to uncover opportunities to strengthen and streamline the process by which cures are discovered and made available to patients.

Cures accelerated the cycle of discovery, development, and delivery of new treatments and ensured that the United States remained at the helm of biomedical innovation. At the National Institutes of Health, the 21st Century Cures Act authorized resources to support biomedical research and reduce administrative burdens and provided almost $5 billion in new funding to support the agency's four innovation projects.

The Precision Medicine Initiative was authorized for $1.4 billion for the National Institutes of Health to build to a national biomedical dataset in order to accelerate health research and medical breakthroughs.

The bill also authorized $1.5 billion for the Brain Research through Advancing Innovative Neurotechnologies Initiative to better understand the brain's physiology and to coordinate efforts across multiple Federal and private groups to expedite research for diseases like Alzheimer's.

Cures also authorized $1.8 billion for cancer prevention, cancer diagnosis, cancer treatment and care through the Beau Biden Cancer Moonshot.

Finally, the Regenerative Medicine Innovation Project was authorized at $30 million to support clinical research in the field of regenerative medicine in coordination with the Food and Drug Administration.

The 21st Century Cures Act helped the Food and Drug Administration modernize the regulation of medical products throughout its lifecycle. It established the FDA Innovation Account and authorized $500 million in funding to implement Title III of the law, which included a broad range of deliverables from the Food and Drug Administration.

These include creating a mechanism for the collection and incorporation of patient perspectives in regulatory decisionmaking, updating the way medical products are reviewed and approved, and advancing new drug therapies through a review pathway for biomarkers and other drug development tools to help shorten the development time while maintaining the same rigorous standard for safety and effectiveness.

It also required the Food and Drug Administration to establish standards and definitions necessary to develop regenerative medicines.

Before I close, I recognize the 21st Century Cures Act also touched upon other critical healthcare priorities, such as mental health and health information technology. Both of these areas should have their own separate hearings because of their importance to the medical community, and those are on the list for the very near future.

I again want to welcome our witnesses and thank you for being here. I look forward to your testimony.

My time has expired, and I will yield to the gentleman from Texas, Mr. Green, the ranking member of the subcommittee, 5 minutes for an opening statement, please.

[The prepared statement of Mr. Burgess follows:]

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Mr. Green. Thank you, Mr. Chairman.

And thank you, Dr. Gottlieb and Dr. Collins, for being here this morning.

And I want to thank former Chairman Upton and Congresswoman DeGette for being the original cosponsors of the 21st Century Cures.

Next month will mark the 1-year anniversary of the 21st Century Cures Act being signed into law by President Obama in his last public signing ceremony. It was a great achievement, particularly at a time of hyperpartisanship and gridlock.

The work started long before 2016. In 2014, we set out on a mission to do something positive to boost medical research and innovation and accelerate the discovery, development, and delivery of new cures and treatments.

After countless hours devoted to roundtables, white papers, hearings, and drafts, Cures enjoyed bipartisan support and endorsements from over 700 organizations representing the full spectrum of stakeholders. It dedicated $6.3 billion in new investments to support priorities like the Beau Biden Cancer Moonshot, the BRAIN Initiative, and the Precision Medicine Initiative within the National Institutes of Health to combat prescription drug abuse.

It also provides money to the FDA to advance the agency's mission and implement the policies in the underlying bill. This influx of investment is being put towards solving today's complex science problems, getting new treatments from the lab table to the bedside, and improving public health. Specifically, the NIH was provided $4.8 billion in new funding to advance cutting-edge research initiatives.

The FDA was provided $500 million over 10 years to improve the agency's medical product review process and expedite patient access to drugs and devices without compromising the safety and effectiveness standards.

In addition to this much needed funding, there were so many provisions in this

package worthy of support, from facilitating development of new antibiotics, the fight against superbugs, to advancing the use of modern clinical trial designs, to fostering the next generation of medical researchers.

While some of the provisions are technical in nature, the real world impact they could have is not abstract. Patients and families deserve to have their elected officials respond to their needs, and this bill was an earnest attempt to do just that.

Like all negotiations and compromises, we didn't get everything we want, there is always more than can be done. But today is an opportunity to hear from the heads of FDA and NIH on implementation of things like patient-focused drug development, medical device innovation, improving science expertise and hiring capacity.

It is only been a year since passage. These things take time. But I know folks out in the respective agencies have been hard at work to get new initiatives off the ground and build on past efforts to advance medical research and development of new science.

While not the focus of today's hearing, Cures also included $1 billion to combat the prescription drug abuse and overdose epidemic. The funding was significant but pales in comparison to what is needed to combat this crisis. There are more Americans dying from this epidemic than were at the height of the AIDS epidemic.

I hope this committee and Congress can fulfill its responsibilities to the American people and provide real and desperately needed funding to fight this epidemic that has raged in communities head-on. The 21st Century Cures demonstrates what we can accomplish when we work across the aisle, and I hope we can do so again.

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

And, Mr. Chairman, I want to yield the remainder of my time to Congresswoman

DeGette.

[The prepared statement of Mr. Green follows:]

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Ms. DeGette. Thank you very much, Mr. Green, for yielding, and thank you for all of your work that you did on Cures. I am going to be sorry not to have you as my seat partner and my partner in issues like this in the next Congress. You have done a wonderful job.

And, Mr. Chairman, I want to thank you, too, for all the work you did on Cures.

Fred Upton of course is my partner and he was our chairman at the time. And we really wanted to do something bold and big when we started conceiving of 21st Century Cures, and I think we achieved that. And so I am looking forward to hearing from our two witnesses today.

Dr. Gottlieb, your agency was a key partner, and I know you have carried on that effort. And of course Dr. Collins was there from the beginning with us, helping us craft this bill.

At one point I remember Dr. Collins said to me, very early on, he said, "You know, we just need to let our young researchers go to conferences." And I said, "If that is all we do, we will have failed."

And we did that and we did so much more. And so we are eager to hear how this bill has had impact in just 1 year, but we are even more eager to hear where we can take it next.

So thanks for all you do. Thanks to all of this committee for working together on this bill. And I yield back.

[The prepared statement of Ms. DeGette follows:]

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

The chair recognizes the chairman of the full committee, the gentleman from Oregon, Mr. Walden, 5 minutes for an opening statement, please.

The Chairman. Thank you, Mr. Chairman. Thanks for having this oversight hearing, if you will, of an incredibly important lifesaving law that was passed in the last Congress in a bipartisan way. I think it was some of the finest work this committee has ever done.

And I know, Dr. Collins and Dr. Gottlieb, you haven't had anything else on your plate in the last year. But I say that facetiously, because you have had a lot, both of you have, and yet you seem to be doing a marvelous job implementing this vast bill and helping move forward to save lives and to improve the lives of families, friends, people we will never know.

And the consequences of this legislation are not confined to this hearing room, they are not confined to the District of Columbia, or even the United States. The research and the progress that will be made in these sectors will affect everyone in the world. This is world changing. My colleagues on both sides of the aisle have done marvelous work getting this done.

Now, my view has always been that once you pass a law, that is just the starting place. I know how difficult it was for Diana DeGette and Fred and Mike and Gene and everybody else to do this. But that was the starting point.

Today we look and say: What is it going forward? How is this working? Are these tools effective? Are there changes that need to be made? We know you are making great progress and we appreciate the terrific work you are doing.

I also want to recognize a very special guest here with us today, we have many in the room, but I want to draw special attention to somebody who has been part of this

journey from the beginning, and that is young Mr. Max.

Max, we are delighted to have you here. You are an extraordinary young man. And we are so very glad that you are here to share in this special birthday appearance of the 21st Century Cures legislation. And it is because of people like you that inspire us to do the best that this committee has to offer, the best work, the best legislation, because we know human lives are at stake.

With that, I am going to put --

[Applause.]

The Chairman. With that, I am going to submit my eloquently written opening statement into the record and defer the balance of my time to the former chairman of the committee, the chairman on Energy now, Fred Upton. And I know there are other members on our side who would like to share in what time remains.

So with that, I yield to the champion of 21st Century Cures and the improvement of people's lives around the world, my friend from Michigan, Mr. Upton.

[The prepared statement of The Chairman follows:]

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Mr. Upton. Well, thank you.

When we began the process of crafting 21st Century Cures 4 years ago, we began with one goal in mind, and that was helping patients and their families. And Diana DeGette, my great partner on the other side of the aisle, and I were inspired to act after hearing from folks in the research community, as well as patients and their families about the need for modernization and more resources at both the NIH and the FDA, to move quickly, bring lifesaving treatments to market.

And all of us had inspirations in our district. For me, it was two sisters, the Kennedy sisters, Brooke and Brielle, who have a rare genetic disease called spinal muscular atrophy, or SMA. Cures provided the NIH and the FDA with billions, tens of billions of dollars in much needed resources so that our Nation's best and brightest could work on finding cures for diseases that impact virtually every single family, whether it be cancer, diabetes, Lupus, or, yes, rare diseases like SMA.

And this hearing is a great thing for lots of reasons. Most notably, it is a reminder of how Republicans and Democrats came together to get a monumental piece of legislation signed into law despite our divided times. Diana worked with me on this as we worked for years and listened and worked to craft the language that would ultimately become law.

The hearing is also a reminder that we have a lot of work still to do. The Kennedy girls, our buddy Max in the front row, along with millions of patients and families across the country are counting on us.

And for that reason, I am immensely glad to welcome both Dr. Collins and Dr. Gottlieb on how the law is being implemented and what we in Congress can do to help that process a long and improve it.

I yield now to the gentlelady from Tennessee, Mrs. Blackburn.

[The prepared statement of Mr. Upton follows:]

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Mrs. Blackburn. Thank you so much.

And we do welcome our witnesses, and we take this as an opportunity to thank you each for the help and the guidance that you have provided in what were then your roles and what are now your roles as we implement 21st Century Cures.

It is so appropriate that we do this hearing because, as you have heard, there was so much more that went into this than just saying let's have people go to conferences or let's try. This was a way to change and reform the review and approval process so that it more adequately meets the innovation that is taking place in healthcare delivery systems.

So we welcome you.

We welcome Max and his bipartisan friends who have joined him this morning. What a great reminder, Max, that they have a reserved seat right there on the front row in sharing the success of this day.

Mr. Chairman, I thank you for the hearing, and I yield back.

[The prepared statement of Mrs. Blackburn follows:]

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The Chairman. And 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 New Jersey, Mr. Pallone, the ranking member of the full committee, 5 minutes, please.

Mr. Pallone. Thank you, Mr. Chairman.

I want to welcome Dr. Collins and Dr. Gottlieb here today to discuss the implementation of the 21st Century Cures Act. While the law addressed several different issues facing our healthcare system, such as the opioid epidemic and mental health, today we will be focusing on the ongoing work at NIH and FDA to implement the provisions of the law aimed at improving the discovery and development of new treatments and cures.

The Cures Act provided new funding to advance cutting-edge research at NIH. I am particularly proud that the law included funding for the Beau Biden Cancer Moonshot Initiative. This initiative aims to accelerate cancer research in America and improve our ability to prevent and detect cancers early on, and the hope is that one day we might find cures for the many different cancers, such as pancreatic cancer, that afflict patients today. I am interested in hearing how NIH is working to achieve this goal.

I am also pleased that the Cures Act invested new funds in the BRAIN Initiative and the Precision Medicine Initiative, which includes the All of Us Research Program. The BRAIN Initiative funds important research on brain disorders, such as Alzheimer's, epilepsy, and traumatic brain injury. And the All of Us Research Program funds a historic effort to gather data from at least a million people that will help lead to the development of personalized therapies rather than one-size-fits-all treatments.

At FDA, the Cures Act aims to bolster the medical product review process in order to get treatment to patients faster while also maintaining FDA's gold standard for safety

and effectiveness. For example, the law granted FDA added authority to develop and utilize new tools to facilitate drug development, provide greater flexibility in the clinical trial process, and support the development of continuous manufacturing.

It also invested in increased patient engagement by encouraging the use of patient experience data in the review process. And the law also provided FDA with $500 million in new funding to ensure the agency has the necessary resources to recruit the best and brightest scientists and effectively implement the law.

And so I look forward to hearing more about the progress the agency has made to date on all of these issues.

And lastly, the Cures Act marked an important step towards the development of new treatments and cures. And I am pleased that the committee was able to work together on a bipartisan basis last Congress to pass this monumental law. And I of course particularly want to thank the chief sponsors, Fred Upton and Diana DeGette.

It is critical that we hold hearings to ensure the law is working as it should and achieving its goals. And I look forward to hearing from our witnesses today and to further discussions on implementation of other provisions of the law.

So I would like to yield the remainder of my time to Representative Lujan.

[The prepared statement of Mr. Pallone follows:]

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Mr. Lujan. I thank the chairman and ranking member for organizing this hearing today and I thank the witnesses for their attendance.

Last Congress we worked together to pass the Comprehensive Addiction and Recovery Act and the 21st Century Cures Act. It is fair to say it was a compromise, not everyone got everything they wanted.

During the debate I pushed and have continued to advocate for more funding and resources to address the deadliest drug crisis in American history. We came together and we advanced legislation to provide $1 billion over 2 years to strengthen the response to this crisis.

Still, 21st Century Cures Act's 2-year funding window creates planning problems for State and local governments. The uncertainty in funding to hire staff or plan beyond 2 years makes it difficult for people on the ground to do the work we are trying to empower them to do.

We must do more. That is why I introduced legislation to extend Cures funding to combat the opioid epidemic for an additional 5 years. Honestly, a 5-year extension of this funding is the minimum we should be doing.

I am grateful to the members of this committee who have cosponsored this bill, and I ask other members to add their voices to this effort. Let's work together to find common ground and move this.

Because this drug crisis is tearing apart the fabric of communities across the country, we must work together to ensure that this important funding does not expire. Too many people are suffering without access to meaningful support systems.

We must also step up our prevention efforts. One long-term avenue for prevention is the development of safe and effective, nonaddictive opioids. We also need to move forward research and treatments that stop the craving of opioids and

alcohol.

Dr. Gottlieb, I communicated with your office on this matter, and I understand the FDA is working with the NIH on a series of meetings to facilitate development of nonaddictive pain treatments. As you are aware, I sent you a letter on this issue. You responded by answering a few of the questions, but not all of the questions. I will be sending the letter again with expectations of more thorough answers and responses to all of the questions, and I will also be submitting them into the record.

Mr. Chairman, thank you for again holding this hearing. And I yield back to Mr. Pallone.

[The prepared statement of Mr. Lujan follows:]

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

This actually concludes member opening statements, and the chair would remind members, pursuant to committee rules, all members' opening statements will be made part of the record.

And again I want to thank and welcome our witnesses for being here today and taking their time to testify before the subcommittee. Each witness will have the opportunity to give an opening statement, and we will follow that with questions from the members.

This morning we are going to hear from Dr. Scott Gottlieb, the Commissioner of the Food and Drug Administration, and Dr. Francis Collins, the Director of the National Institutes of Health.

Dr. Gottlieb, we appreciate you being here today. Dr. Gottlieb, you are recognized for 5 minutes, please.

**STATEMENTS OF THE HONORABLE SCOTT GOTTLIEB, M.D., COMMISSIONER, FOOD AND DRUG ADMINISTRATION; AND THE HONORABLE FRANCIS COLLINS, M.D., DIRECTOR, NATIONAL INSTITUTES OF HEALTH**

**STATEMENT OF SCOTT GOTTLIEB**

Dr. Gottlieb. Thank you, Chairman Burgess, Ranking Member Green, members of the subcommittee. Thank you for the opportunity to testify today on the anniversary of the 21st Century Cures Act and to update you on FDA's progress in implementing the provisions of this landmark legislation.

The Cures Act gave FDA a broad new set of authorities and resources to adapt our policies and our organizational structure to make sure that our efforts are as modern and transformative as the medical products that we are seeing.

Congress wanted us to have a strong workforce and policies that will enable the America people to capitalize on the breakthrough science that is transforming medicine.

I am proud that my colleagues at FDA have worked hard to meet the commitments under the statute. And I want to commit to you that timely implementation of this legislation is one of my highest priorities. The Cures Act is a defining element of my own policy planning at FDA.

When I arrived at FDA 7 months ago, I remarked that I couldn't imagine a better time to be leading the agency, owing to two important new opportunities. The first were opportunities offered by new science and technology. Gene and cellular therapies, more targeted drugs, regenerative medicine, digital health tools, and new biomaterials offer the potential for dramatically better and even curative therapies for

many disorders.

The second were opportunities provided by Congress. The reauthorization of the user fees and, more notably, the Cures Act offer FDA a new platform to fashion these scientific advances into practical treatments for patients. If I came before Congress 5 years ago and said that within the next 5 years we might have a cure for sickle cell disease or hemophilia or common early stage cancers, such predictions would have been unrealistic.

Such discussions are no longer imprudent. In fact, we should expect these opportunities. While these scientific advances won't be risk-free, these and equally profound clinical opportunities are before us.

The Cures Act inspired a new approach to our work. It was a direction from Congress that you wanted us to think differently when it came to the potential for breakthroughs that could transform human health.

We pledge to remain steadfast to our gold standard for safety and efficacy, but at the same time you asked us to look for ways that we can make our approach to the development of breakthrough products more scientifically modern and efficient to meet the urgent needs of patients.

We have taken the spirit of Cures and set out to extend this directive across our own policymaking and planning. To build on what you asked to do, we will soon release a document that will take full measure of how we are expanding on the provisions of Cures to make sure we are continuing to expand on what Congress set out to achieve.

I want to share with you today one such effort. With the advent of more targeted medicines, we are sometimes able to observe earlier in some cases outsized benefits. This is especially true when it comes to the field of oncology. These situations are compelling us to explore new ways to facilitate and expedite the

development and review of these products.

For example, we are currently examining approaches to better expediting review and approval of these products by leveraging FDA's existing expedited programs. Accelerated approval has typically been granted in circumstances where earlier stage or smaller datasets show benefit for a serious unmet medical need. But that showing of benefit is typically based on the drug's effect on a surrogate endpoint. In these cases that endpoint, like tumor shrinkage, is judged to be reasonably likely to predict clinical benefit.

What do you do when we have a targeted drug introduced into a properly selected group of patients which has an outsized benefit on overall survival in a rare or deadly cancer, but where that benefit is seen in a small trial where we would still need more evidence to fully understand how to best use the drug in clinical practice?

We might want to approve such a product earlier and require a post-market confirmatory study to validate the finding, similar to an accelerated approval approach.

Even though the observed benefit in this case is on a clinical endpoint, an early look at survival, and not on a surrogate measure of benefit, we believe using an accelerated approval approach could often be valuable.

Congress clarified our authority under FDASIA to grant accelerated approval based on intermediate clinical endpoints. We want to better define what is meant by intermediate endpoints to ensure that product developers with promising drugs take full advantage of this provision and can consider it in a broader range of such settings.

As the mechanism of diseases like cancer become more clearly defined and drugs targeting these conditions more carefully tailored to the underlying biology of the disease, we are going to see more such cases, situations where a new drug offers an outsized survival benefit in a selected population of patients in a smaller earlier stage

clinical trial.

One reason we want to consider accelerated approval in these setting is that it would include authority to require confirmatory evidence to support the continued marketing of the drug and an expedited withdrawal mechanism if that evidence fails to confirm the benefit. We intend to further explore the application of these principles in additional policy work we are undertaking.

To fully leverage these opportunities and in keeping with the spirit of Cures we are working on a similar proposal. For cancer drugs already approved for one indication, approval for a supplemental application, where the approval concerns a second indication, can sometimes appropriately rely on a more targeted dataset like a single arm study. We intend to issue guidance further clarifying the circumstances in which this is appropriate.

In closing, this may be suitable, for example, when there is a clear and outsized treatment effect and the second indication concerns the same disease as the first one but for on new setting, for example, a targeted drug approved for a third line use that shows benefit in a second line indication.

Cures refashioned and modernized FDA's footprint, enabling new technologies to reach patients more efficiently, giving the agency new authorities and resources to invest in our workforce, and it shapes our spirit of our mission. We will continue to build on its framework.

I look forward to discussing our plans to fulfill and expand on these opportunities, and I look forward to answering your questions.

[The prepared statement of Dr. Gottlieb follows:]

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Mr. Burgess. The chair thanks the gentleman.

The chair now recognizes the Director of the National Institutes of Health, Dr. Collins, 5 minutes for an opening statement, please.

**STATEMENT OF FRANCIS COLLINS**

Dr. Collins. Good morning, Chairman Burgess, Ranking Member Green, other distinguished committee members. It is an honor to be here today with my colleague, Dr. Scott Gottlieb, the FDA Commissioner.

We were cheering a year ago today, November 30, when the Cures Act passed the House of Representatives 392 to 26. And as you well know, this act aimed to catalyze a very important goal shared by all Americans: to speed the pace at which scientific discoveries are translated into lifesaving treatments and cures. And I am here to talk to you today about how that dream is coming true.

We at NIH greatly appreciate your leadership in passing this bipartisan act 1 year ago that enhances our authorities and our resources in ways that will help us to achieve this goal. Many thoughtful provisions are included in the act, such as reducing administrative burdens so our scientists can devote more of their time to research, expanding our ability to award prizes for exceptionally creative ideas, and strengthening measures to protect patient privacy when individuals are involved in research.

In my written statement I have submitted a comprehensive report on how NIH has worked quickly to implement the provisions of the Act. We are motivated by a sense of urgency to help patients in need of breakthroughs. In my oral statement just now, I would like to focus on the Cures Innovation Fund.

Among the vital areas of NIH-supported research being accelerated by this fund

are the BRAIN Initiative, the Cancer Moonshot, the Regenerative Medicine Innovation Project, and the Precision Medicine Initiative. I am also delighted to have Max here representing the most important audience for anything we are talking about today, which are those patients who are waiting for answers to conditions that need those answers. And I would also like to recognize my friend Doug Oliver, at the end of the front row, who has been a very effective spokesperson for the importance of investing in regenerative medicine.

Let's begin with the BRAIN Initiative. This pioneering effort is aimed at revolutionizing our understanding of the most complex structure in the known universe, the human brain. In fiscal year 2017, we leveraged our Cures innovation funding with our annual appropriation to launch no less than 110 exciting new brain research projects.

Some of these will develop detailed maps of neural circuits, others will create a census of cell types in the brain, and still others will create powerful new tools to monitor and modulate brain activities. This will advance efforts to develop new ways of detecting, treating, and even preventing many serious brain disorders, such as Alzheimer's disease, Parkinson's, schizophrenia, autism, drug addiction, epilepsy, and traumatic brain injury.

With the help of the Cures Innovation Fund, a second research area, the Cancer Moonshot, is aggressively pursuing a very ambitious goal: to accelerate advances in cancer prevention, diagnosis, treatment and care, in collaboration with our good colleagues at FDA.

To achieve that goal we must take a variety of innovative steps. These include enhancing the research infrastructure by creating a clinical trials network, with an unwavering commitment today to sharing, to move cancer treatment programs forward rapidly.

In another innovative move, NIH recently joined with the FDA and 12 pharmaceutical companies to launch the Partnership for Accelerating Cancer Therapies, or PACT. This public-private partnership will initially develop biomarkers to speed the development of cancer immunotherapies, an exciting new approach to treatment that enlists a patient's own immune system.

Recently, we have seen some amazing responses from immunotherapy, but we need to bring that kind of success to far more people with more types of cancer and do it quickly. The Cures Innovation Fund, with the support of this Congress, is helping to make that happen.

The Cures Act also provides support for regenerative medicine research. This emerging area of science includes the use of cells and other technologies, such as engineered biomaterials and gene editing, to repair or replace damaged cells, tissues, or even whole organs.

A result of the Cures Act, NIH has launched the Regenerative Medicine Innovation Project. This project recently made eight clinical research awards covering a broad spectrum of science and technology, and going well beyond the funding specifically provided by the Cures Act, because we found it to be so compelling.

Some are focused on common diseases, including diabetes and vision disorders, while others are aimed at rarer conditions, such as sickle cell disease, which Scott has already mentioned is a very exciting time of potentially moving forward to cure in as little as 5 years, and a condition like idiopathic pulmonary fibrosis, and many others.

Also, in partnership with the FDA, we are going to be hosting a workshop next week which is going to explore the state of regenerative medicine research involving adult stem cells. This conference will inform our future research directions by helping us to identify areas of greatest scientific and therapeutic promise.

Finally, I want to tell you how I thrilled I am that you supported the Precision Medicine Initiative, PMI, by including an authorization and funding in the Cures Act.

The centerpiece of PMI is the All of Us Research Program, which will enroll 1 million or more Americans from every walk of life. These volunteers will contribute their health data in many ways, over many years, to create a research resource that will catalyze a new era of precision medicine.

This is a truly ambitious goal, and we know that NIH cannot succeed on its own. So all across the nation, NIH is teaming up with the Veterans Administration, health provider organizations, community health centers, and other groups -- recently libraries all across the country -- to figure out the best ways to recruit participants, especially those that are traditionally underrepresented in biomedical research.

NIH has also partnered with five companies to create a participant technology center, and our partners are testing how wearable devices, like the ones I am wearing today, and many of you are probably wearing something like this, how can we use these to provide easy ways for all of us volunteers to contribute data on physical activity, sleep, heart rates, environmental exposures, and so on.

Getting all these partners on board would have been nearly impossible had not the Cures Act included something called Other Transactions Authority for PMI, making it possible for NIH to move forward with unprecedented speed and flexibility to carry out beta testing of all the many components, and now a planned launch in the spring of 2018.

As someone who grew up in a theater family, I know the value of a dress rehearsal before the curtain goes up. That is what a beta test is. But when it does go up, you and everyone else who supported the 21st Century Cures Act will deserve applause, not just for all of us, but for each of the many, many ways in which Cures supports the work of the National Institutes of Health, or as some have called us, the National Institutes of

Hope.

Speaking of hope, let me conclude with a favorite exhortation from the poet Peter Levi: Hope in every sphere of life is a privilege that attaches to action. No action, no hope.

So thank you for your action in enacting Cures. Thank you. I will be happy to answer your questions.

[The prepared statement of Dr. Collins follows:]

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Mr. Burgess. The chair thanks both of our witnesses for their testimony, and we will move into the member question portion of the hearing.

I actually want to recognize the chairman of the full committee, Mr. Walden from Oregon, for 5 minutes.

The Chairman. I thank the chairman.

And again thank you both, not only for your good work, but also your terrific testimony here today.

And I also want to thank Dr. Gottlieb for his excellent efforts to make sure that our warfighters have access to cutting-edge medical devices and medicines that are both effective for them and safe for them. We appreciate the work you did with us and our friends at the Armed Services Committee and Pentagon to get that done.

Dr. Gottlieb, the FDA Oncology Center of Excellence was created in Cures as a model of how collaboration in science among and within government agencies should be done in the future. This is a new model, and I know we were hoping here in Congress that this would succeed. And in your testimony you reference the role of OCE in the review and approval of two cell-based gene therapies that are indicated for treatment of cancer patients.

Can you speak a little bit more about how groundbreaking these two treatments are and the role OCE played in their approval?

Dr. Gottlieb. Thank you, Mr. Chairman.

I just want to make one brief comment about the legislation that this committee helped craft and crafted with respect to the warfighter. I think it is going to give us a profound opportunity to expedite the approval of products destined for the battlefield setting and to help protect and promote the health of warfighters in the battlefield setting.

We look forward to early implementation of that and robust implementation of that. We will try to make an effort early on to put out specifications on how we plan to make full use of that. I think it is going to provide a profound opportunity for our warfighters, and I thank the committee.

With respect to the Oncology Center for Excellence, the products that you refer to were gene therapy products that we think are going to represent sort of a transformative opportunity as a class of products for the treatment of patients with a range of conditions, including cancer. These were CAR-T products where cells are genetically altered to attack cancer and personalize to the patient's individual cancer.

With respect to the Oncology Center for Excellence, it was instrumental in the review of these products. We believe that the orientation for the future across the entire agency is to try to consolidate the clinical portion of the review among the agency's various medical product centers.

We divide medical products into different centers, but the clinical aspects of the review remain the same, even if the product features are different. And so trying to consolidate that clinical portion of review provides a lot of efficiency, rigor, and also helps quicken the process. And so standing up this new oncology center we think is critical to the future of these classes of products.

The Chairman. Thank you, sir.

Dr. Collins, over the last several years NIH has been acting to address a biomedical research workforce that is tilted toward, frankly, late-career investigators. The population of grant recipients is highly concentrated, with 10 percent of NIH-funded investigators receiving over 40 percent of NIH funding.

Analyses conducted by your agency and others have shown that a more diverse population of NIH grant recipients would be beneficial to biomedical research. Cures

required the NIH to develop strategies to promote and facilitate the next wave of young researchers, and in your testimony you talk about the Next Generation Researchers Initiative.

Can you further elaborate on the multipronged approach you plan to take to increase the number of NIH-funded early stage and mid-career investigators.

Dr. Collins. Thank you for the question. This is an area of great and high priority for us, and we appreciated very much the way in which the Cures bill called this out and gave us additional encouragement to think boldly about how we can be sure this next generation of researchers are getting their start as independent investigators with all of the energy and creativity that they bring to it.

And we could look at our own demographics and see that we were increasingly seeing an aging of our workforce. And while we have many investigators who are highly productive as senior investigators, we were worried that the next generation was having a tough time coming on board.

So over the course of this past year since the Cures Act passed, and guided by many conversations before that, we have come up with an approach which is going to provide additional resources for those who come to us for the first time with a grant that has not previously been funded by NIH, but this is their start, and to provide additional opportunities for those individuals, if they fall in the top 25 percent of applicants, to be able to receive funding.

We made this decision fairly late in fiscal year 2017, but we were determined to go ahead and implement it. We are still in the process of identifying all of those investigators who were reviewed in fiscal year 2017 that otherwise would have missed the cut, but whom we now believe we can reach down to and find funds for.

And we are also very concerned about those who are at risk of losing all of their

funding. They got started into the pathway, they came back for their competing renewal, just missed the cut, and without that they may have to close their labs and do something else. We are also seeking then to identify those individuals and give them an additional boost.

Now, that money has to come from somewhere, and that means that we may not be able to be quite as generous in other areas of research, including some labs that are extremely well-funded, and as you can imagine, not everybody has been excited about that part.

But we do believe it is the right thing to do. This is the future. If our mission is to try to find every place that we can to use the dollars that the Congress provides us to get the maximum benefit, those young investigators just getting started are a critical part of that.

The Chairman. Thank you.

Thank you both for the good work you are doing and for being here today before the committee.

With that, Mr. Chairman, I yield back.

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

The chair recognizes the gentleman from Texas, Mr. Green, 5 minutes for questions, please.

Mr. Green. Thank you, Mr. Chairman.

Over the last decade there has been a growing recognition in the U.S. and abroad that antibiotic resistance poses a serious and growing threat to our health. Antibiotics are the underpinning of modern medicine. Without them important medical advances such as chemotherapy and surgeries become very risky because of the possibility of infection.

Addressing this threat requires a multipronged approach, including reducing the inappropriate use of antibiotics in human healthcare and agricultural settings and developing new antibiotics and other therapies. We know that there are a number of challenges in discovering and developing new antibiotics.

Dr. Collins, my first question. There are basic scientific barriers which impede new antibiotic discovery and development. Can you tell us what the NIH is currently doing and will be doing to address these barriers?

Dr. Collins. We have a very important role to play. So thank you for the question.

Yes, there have been challenges in terms of keeping this pipeline of discovery and development going for antibiotics, in part because some sort of looked at this as a bit of a market failure because of the expectation that new antibiotics would have potentially a very limited market for a while. You would want to save them for those circumstances where you really needed them.

So NIH has an even larger role to play in this space in terms of the discovery part and in moving the new discoveries along the pipeline closer to commercialization, to de-risk those projects, so that antibiotics will be seen by the commercial sector as something that they are ready to pick up and go. And we at NIH, particularly through the National Institute of Allergy and Infectious Diseases, led by Tony Fauci, have a very significant amount of funding invested in this space.

There have been some exciting developments. One is basically using new technologies to discover naturally occurring antibiotics that are created by soil organisms that we didn't previously know were there because we can't culture them in the lab, but new technologies have made that possible. There is a whole new generation of ideas coming from there.

But this is not a solved problem. I am glad you are raising it. It is going to take the full effort of the public and the private sector, supported by this Congress, to be sure that we are inspiring the maximum energy in this space, because we have a ticking clock here for a significant number of individuals who are being found with infections for which none of our antibiotics currently would be able to work.

Mr. Green. Well, we will not be able to succeed in the goal of developing antibiotics without a strong bench of scientists. What is NIH doing to ensure that these young scientists are pursuing careers in the antibiotic discovery and development?

Dr. Collins. Well, this ties into the answer I gave a moment ago to Chairman Walden about the things that we are doing to try to encourage our first-time investigators to come on board and to be able to get successfully funded. And in fact many of those investigators are in this area of infectious disease. So as we are lifting all the boats for that category of investigators, we are also helping in this space.

But the National Institute of Allergy and Infectious Diseases also, because this is a high priority, issues special funding announcements, specifically recruiting investigators to work in this space, recognizing that there are people out there who might just work on something else, but knowing that there is a funding opportunity, would raise their hands and say, let's work on this. And we have to do all those things together.

Mr. Green. Dr. Gottlieb, this committee has taken the threat of antibiotic resistance very seriously. In 2012, Congress passed the Generating Antibiotics Now Act, the GAIN Act, which our former colleague, Phil Gingrey, who is here today. It came out of this committee and gave exclusivity to new antibiotics to treat serious and life-threatening infections.

Just last year in Cures we passed the ADAPT, which created a new regulatory pathway for antibiotics that treat serious and life-threatening infections and meet an

unmet need. I thank Congressman Shimkus for picking up that, cosponsoring. Can you give us a status update on implementation of ADAPT?

Dr. Gottlieb. It continues to move forward.

I will comment on a couple things, if I may, Congressman. To answer, to pick up an earlier comment you made, we are going to continue to take steps to try to reduce antibiotic use in veterinary animals. We have taken steps, as you know, to put them under veterinary supervision. And we are going to look at continued steps we can take to address some of the prevention claims in those labels and build on the good work that was begun by my predecessor, Dr. Hamburg.

Another important provision -- you mentioned the GAIN Act -- another important provision is obviously the LPAD designation that was created by the Cures Act. We are going to put out guidance on that this summer. We have had a large number of -- or a limited number, but a robust number given the early days of that provision -- pre-IND meetings with sponsors that are looking to take advance of that provision as a way to accelerate the approval of products targeted to resistant organisms.

So I want to thank the committee for the collective good work that you have done through all of this legislation. This has been immensely important to the agency in giving us a new set of tools to address these issues.

Mr. Green. Thank you. And I don't have anymore time left. But, again, thank you for that effort.

And thank both of your being here today and the work you are doing. And, obviously, as a committee we want to continue to partner with you.

Mr. Guthrie. [Presiding.] Thank you. The gentleman's time has expired. And I will recognize myself for 5 minutes for questions.

Thanks, Dr. Collins, Dr. Gottlieb, for being here.

When I am home a lot of times doing townhalls or whatever, a lot of times most of the things I talk about is what is happening from this subcommittee in the healthcare world and the research. It is just fascinating stuff that is going on. As Dr. Gottlieb said, we are talking about being able to hopefully be on the cusp of curing diseases we never thought about.

I remember about this time last year the roundtable where Roger Daltrey was here. He was talking about teenage cancer. We also had a young man who was talking about cystic fibrosis. And I have a friend who lost his son in his mid-twenties to cystic fibrosis.

So I was sitting there thinking about, wow, he is young, my daughter's age, and where we were a few years ago he probably had just a few years left to live. And depending on a lot of circumstances, but they talked about he may live a full life expectancy. And that is really what is happening with the research at NIH, what is happening in the private sector.

And so I think for me what made 21st Century Cures exciting -- and all of us have these experiences -- I had a constituent whose son has Duchenne -- or a constituent that has it -- his father -- that has Duchenne Muscular Dystrophy, who would come to our office and say, "There is this promising trial. My son is not in the trial. But it doesn't improve you, but it prevents you from regressing." So he was racing against time for his son not to get into a wheelchair, because his goal was for his son not to be in a wheelchair.

Another one, a constituent called crying whose son was on the trial for the artificial pancreas. And then the trial was over. Of course, it was in a lab setting, so they couldn't take it home. And she said, "My son has never felt this good since he was diagnosed, and now I have got to give this up. They have it back now because it has

been approved."

And I felt that because I had a child with little childhood issues, and parents immediately become experts in the information around that childhood disease, it just drives your life, I can tell you that.

And so we hear from a lot of people, and what we want to be able to say with confidence is that the research -- the money we are appropriating has been spent correctly, which I feel confident with your leadership at NIH.

And, Dr. Gottlieb, we want to make sure that the FDA is doing everything to get these.

Because if you are a parent and you are not in the clinical trial, but you are hearing that, "Well, this is for a small basis, but we are not sure I can extrapolate along the whole population," I mean, you want it for your child if you can have it, but understand the safety and the efficiency that you guys have.

And so what we wanted to do, my view of what 21st Century Cures is all about, how do we give you the tools in your research and in your approval process to make sure that people in those situations are confident that it is coming as fast as possible, if we have to accelerate the approval process in those things moving forward.

And so I am excited for this overview, because I think this is an example -- we have Mr. Upton and Ms. DeGette, who were the cosponsors, 392 to 20-something I think was the count -- that it is something that drives all of us here in Washington, because we all these experiences personally or with our constituents.

And the one area that I focused on, and it was the continuous manufacturing, that is kind of my background. So, Dr. Gottlieb, I appreciate you being here. And I understand the development of continuous manufacturing systems could be some of the most significant developments in the pharmaceutical industry in the next decade. And I

am happy to hear that FDA is taking steps to facilitate progress in this arena so that our country can recognize the benefits of this faster, in a more reliable way to manufacture pharmaceuticals.

Can you speak to the next steps in this arena? And will you be providing additional grants? And how do you envision this technology improving in the field?

Dr. Gottlieb. Thank you for the question, Congressman.

As you know, this committee provided us a good head start in trying to facilitate the continued development of this very important technology, as you rightly noted, providing grants for the development of tools that will help this technology continue to advance.

We have allocated one such grant of I believe a million dollars. We have about $4 million left to allocate, we are going to do that, to look at other programs, mostly in academic institutions, that can help facilitate the development of the regulatory tools that we will use to better evaluate and allow this technology to advance.

This is very important, you mentioned, to allowing more efficient, maybe lower cost development or manufacturing. It also is very important to trying to address drug shortages. Because of the nature of continuous manufacturing you don't have as much risk of discontinuities in the manufacturing process as you would through traditional manufacturing.

And the final point I would make is that by using continuous manufacturing you require a much smaller, less expensive footprint. So I think that the rapid deployment or the further deployment of this technology is going to lend itself to potentially repatriating some of the manufacturing that we have seen go offshore coming back to the United States.

And a final thought is that I think this technology is going to be very important to

some of the newer, more complex products that we see in development, like gene therapy. So we think of continuous manufacturing with respect to small molecules. It is also being adopted with respect to biologics as well.

Mr. Guthrie. Well, thank you. As I said, as my friend's son with Duchenne, they are racing against time, so speed is important. But the regulatory side is important, too, as I understand that, as well.

My time has expired. I would like to recognize the ranking member of the full committee, Mr. Pallone, for 5 minutes for questions.

Mr. Pallone. Thank you, Mr. Chairman. You already actually asked one of my questions, so I have to cut that out.

But let me start out with Dr. Collins, and then I will go back to Dr. Gottlieb about continuous manufacturing, if I could.

Dr. Collins, during the 21st Century Cures debate we had a lot of discussion about the future of the biomedical research workforce and its importance to the U.S. remaining the world leader in biomedical innovation. While I am glad that we are able to work together to advance policies that support the development of the next generation of researchers, I am concerned about reports on how the House tax bill could thwart such efforts.

As you know, a fundamental element in pursuing careers in biomedical research is obtaining a graduate degree. Unfortunately, the House tax bill could put such education out of reach for students. According to my own Rutgers University president, Dr. Robert Barchi, the provision of the House tax bill that would tax as income tuition that schools waive for graduate students working as teaching or research assistants, would impose -- and this is a quote from the Rutgers president -- would impose an especially heavy burden on our graduate students, many in STEM fields.

Other college leaders have said that the change will make graduate education unaffordable, lead to fewer graduate students at time when the U.S. needs more students

earning advanced degrees in the STEM fields to remain competitive.

So I just wanted to ask you, are you worried that making tuition waivers taxable income for graduate students would harm our efforts to create the next generation of scientists? And how might such a result harm our ability to advance the discovery and development of new treatments in Cures, which of course was the galvanizing force behind 21st Century Cures, if you would?

Dr. Collins. Congressman, thank you for the question, and it ties in with what I was saying a few minutes ago responding to Chairman Walden about the Next Generation Researchers Initiative, which we are putting a lot of time and effort into trying to be sure becomes a high priority.

Certainly graduate students as the path towards those independent investigators of the future are absolutely critical, and we want to have all the best and brightest who are interested in pursuing those careers to have the opportunity to do so. And anything that represents a major impediment in that regard is something we should take with great seriousness.

I am not an expert in tax reform or in the particular provisions of any of the bills that are under consideration, but certainly I think we can all agree that given that science has driven our economy in this country -- by most estimates more than 50 percent of our gross since World War II has been on the basis of science and technology -- this is a very important area for continued investment. And anything that would diminish the interest and the talent of the next generation in joining that workforce is something we should be very cautious and careful about.

Mr. Pallone. I appreciate that. Thank you.

So let me go back to Dr. Gottlieb. I know that Mr. Guthrie talked about the continuous manufacturing issue. And you mentioned, I think, Dr. Gottlieb, that you awarded the first continuous manufacturing grant in this fiscal year, I guess to the University of Connecticut, to build a manufacturing platform for complex dosage forms.

What I wanted to ask though is, will you discuss further how many additional grant awards the agency intends to offer and what criteria the agency is considering when awarding these grants for the continuous manufacturing?

Dr. Gottlieb. Thank you for the question.

I mentioned we had $5 million to allocate. We allocated a million dollars of it and we are going to continue to allocate the other $4 million. I am not quite certain how many different grants we will give, but there will certainly be a number of grants awarded. And there are a number of academic institutions doing good work in this area, including one in my hometown of Rutgers University, that has a program looking at this.

The criteria we look at are programs that are developing regulatory tools that can serve the basis for how we are going to evaluate this technology when sponsors bring in applications where they are employing continuous manufacturing. So because it is so novel, it requires us to think differently about how we apply our own regulatory oversight to the manufacturing process, and that is going to also require us to develop new methodologies, new SOPs, but also new tools to evaluate the safety and reliability of the manufacturing process.

And so we are looking for institutions that are helping to develop those tools. As I mentioned, there are a number of them, including one in my hometown, but UConn also had a good program in doing this.

Mr. Pallone. Thank you so much.

Thank you, Mr. Chairman.

Mr. Burgess. [Presiding.] The chair thanks the gentleman. The gentleman yields back.

The chair recognizes the gentleman from Michigan, Mr. Upton, the primary sponsor of the Cures bill, 5 minutes for your questions, please.

Mr. Upton. Well, thank you, Mr. Chairman.

I know that Diana DeGette and I appreciate all the kind words here today, but I just want to remind everyone that it was everyone on this committee as we passed it 51 to nothing. We had wonderful staff who worked plenty of weekends for lots of the year. We had a leadership on both sides of the aisle. We had an administration. And we had the appropriators. So together we did this, and it was a great victory for sure.

And I know a number of us were at the Ken Burns dinner earlier this week, and I am very proud to say that he is working on a documentary on the NIH that he will be unveiling I believe next year through PBS. And I talked with Dr. Collins earlier in the week. I know that they have done some extensive filming already.

I think that it is important for the American public to see, in a nonbiased way, the great work that the NIH has done and is going to do. And, obviously, this legislation is going to find the cures that so many families desperately want.

I would like to start off just by asking Dr. Collins to explore a little bit more of the All of Us Project. To me, this is exciting. I know a little bit about it. I know that the unveiling is scheduled for next spring. I have some concerns about the privacy element of it in terms of what the individuals themselves will experience or some of the protections that might be there.

How can we help? And tell us a little bit more about it and what it is going to be able to do.

RPTR PETERS

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[11:03 a.m.]

Dr. Collins. Glad to. And I appreciate your strong support, and that of this entire committee, for the concept that we are trying to pursue here, which is the largest-ever contemplated longitudinal cohort study in the United States of individuals across a wide diversity of ages, ethnicity, socioeconomic status, race, and so on.

And this is going to be a platform for discovery for almost everything you want to know about what allows people to stay healthy, and what happens when illness strikes, and how can we best take care of it.

I appreciate your mention of the Ken Burns film, by the way. And I hope members of this committee had a chance to see, earlier this year, the "First in Human" series that was 6 hours on Discovery Channel about what it is like to be involved in a clinical trial at the NIH Clinical Center and what goes through all those experiences in terms of trying to find answers for untreatable diseases. It was inspiring and emotionally powerful.

The All of Us Program is really a dream for many of us that we have had maybe for a couple of decades but has only become recently practical. We are counting on this million strong group of Americans to be our full partners. As I mentioned in the opening statement, we are doing a beta test right now. We have enrolled about 9,500 individuals just to see how the pieces of this are going to work.

Mr. Upton. And how long does that beta test take? I mean, for the individual when they come in. Is it a blood sample? What does is it that they do?

Dr. Collins. It is blood sample. It is a series of fairly simple physical

measurements. It is answering a whole series of questions in a questionnaire at your own convenience. And it is, of course, a detailed consent process so that people know what, in fact, they are getting into.

You asked about privacy. And everybody is worried about that. And we are as well. And this is a program that has to maintain the highest standards of privacy and security in order to be credible. And we are working with partners that are top of the market here in terms of doing that. One of our major partners is, in fact, Verily and Google.

And all of the patient identifiers are stripped off before any of the data is actually moved into a location where researchers have access to it, and everything is encrypted end to end. We have already been doing a series of penetration tests and hack-a-thons to see whether there are weak spots in this enterprise. And so far it is looking really good.

But we are not going to do the full launch until we are absolutely convinced that all of those parameters have been taken care of.

Mr. Upton. So when that volunteer participates in the program, how often will you come back to that individual? And what information will they continue to transmit over the rest of their lifetime?

Dr. Collins. That is critical, because we do want people to feel like this is something they are proud to be part of it, it is giving them information back. Retention is going to be critical over decades.

So they will be getting information back about themselves in terms of blood test results, ultimately their DNA analysis, which is going to get started sometime next year, as well as giving them information about how they fit in with the rest of this million-strong people.

So we will be in touch with them at least every couple of months, seeking constantly to hear from them, what they like, what they don't like. They are really at the table here in designing this with us.

Mr. Upton. So a lot of us very familiar with the private group 23andMe.

Dr. Collins. Oh, yeah.

Mr. Upton. Where people actually send their saliva. Is this going to be somewhat similar to that? Is it going to be more extensive?

Dr. Collins. So 23andMe is a commercial operation which many of us, including myself, have taken advantage of. It does give people genetic information back. We have learned a lot from them in terms of how they do their educational materials to explain things that can be a little complicated in a sensible fashion that people can absorb.

But we are going to give more than that. We are also interested in environmental exposure.

Mr. Upton. I know my time is rapidly expiring. But I know that your predecessor we worked with at the FDA on 23andMe to make sure that this could actually be launched in a successful way. So I presume that you will be working very closely with the FDA on this to make sure that it meets all the proper requirements.

Dr. Collins. So FDA has worked, I think, very effectively in this space, if I can speak for my colleague here, in terms of figuring out how to do the right balance between protecting consumers against fly-by-night genetic tests that are giving you inaccurate information versus those where people are really interested. And I think they have got the balance just right.

Dr. Gottlieb. And also trying to develop a framework. We have taken a firm base approach to the regulation of these kinds of consumer genetic testing technologies

and announced that about 2 weeks ago, where we are going to allow the test platforms themselves to iterate and regulate the firm itself to make sure it has good SOPs in place and then allow them allow them to go to market with iterations to their test the same way we approach digital health.

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

The chair recognizes the gentlelady from Illinois, Ms. Schakowsky, 5 minutes for questions, please.

Ms. Schakowsky. Thank you so much. I really appreciate, Dr. Collins and Dr. Gottlieb, for your being here today.

One of the most critical components of the 21st Century Cures Act was providing the NIH with the $4.8 billion in new funding. And these dollars are certainly critical in advancing research and many meaningful initiatives, like precision medicine and the Cancer Moonshot, as you mentioned, Dr. Collins.

But we must have a serious conversation about drug prices and we need to do more to address this growing problem. If we are spending billions to incentivize the development of new drugs, I think we also have to ensure that patients can afford those drugs.

The development of new drugs and devices is meaningless unless the discoveries are affordable to patients. It is almost cruel to find a cure and then have it priced so high that a patient can't afford it.

I hear from my constituents that the cost of the drugs that they pay for, that they need, is far too high, and that they are frustrated that they are paying twice for their prescription drugs, once in taxpayer dollars, funding for drug discoveries, and then again at the pharmacy.

So, Dr. Collins, here is my question. I know that scientists dedicated their lives,

your life, to make discoveries that make the world a better and healthier place. As NIH is funding research that will lead to the development of therapies, do you think that patients should be able to afford the drugs that result from your NIH-funded research and that hard work?

Dr. Collins. So this is, obviously, a topic that is on many people's minds. The designate for HHS Secretary yesterday said, yes, we do have a problem with drug pricing. Everybody agrees that this is a serious issue.

NIH has some roles to play but not to the degree that perhaps the public wishes or you might wish that we do. What we can do is to try to be sure that we are doing the front end of drug discovery, which is to identify the right targets and then to develop a pathway towards turning those into therapeutics as efficiently and accurately as possible so that the failure rate for drug development is not so incredibly high as it currently is.

One of the reasons that drugs are so expensive is because the industry has to compensate for all those failures, which are over 95 percent depending on how you count. If we had a success rate of, let's say, 50 percent instead of 5 percent, you can imagine how the equation would look a lot different.

Our goal -- and the National Center for Advancing Translational Sciences, NCATS, is a big part of that -- is to try to do better in terms of identifying ways to be more efficient, ways that we could do toxicology more cheaply, and other things such as that.

But when it comes to actually having a role in determining the cost, the price of a drug once it has left NIH's hands, it has been commercialized -- which it needs to be, we don't make pills -- we don't really have any levers to pull in that situation. We depend on other places to do so.

Ms. Schakowsky. Well, let me ask you this. First of all, you mentioned a kind of calculation, how many failures there are. We do not know that. We have asked for

transparency of how much is actually spent to develop. We would like to see that data.

But has the NIH ever exercised what I think is its right under these licenses to ensure that publicly funded drugs are reasonably priced?

Dr. Collins. I believe you are referring to the march-in rights, which are a component of the Bayh-Dole Act. We have looked at that and have been asked on a couple of occasions to see whether that would apply in a case where a drug price seems to be unduly high and NIH has played some role in its early development.

But if you look at the language of the bill, it really intends to cover a circumstance where a drug is simply not available to the public under any circumstances, and then NIH is entitled to step in. This is a little different when it is available but at high cost. Our legal experts don't feel that the law actually puts us in a position to step in.

Ms. Schakowsky. I thank you for that. I do understand that it is outside NIH's purview to always ensure that the drugs are reasonably priced. But, really, I think we need to be partners in figuring out this piece, because I believe that some of the calculations and some of the prices really do say that many people are not going to be able to access the cures that are available that are shortening their lives. So I appreciate that. Thank you.

Dr. Collins. Glad to work with you in any way we can.

Ms. Schakowsky. I yield back.

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

The chair recognizes the gentleman from Illinois, Mr. Shimkus, 5 minutes for questions, please.

Mr. Shimkus. Thank you, Mr. Chairman.

Again, welcome. We are glad to have you here. Kind of an exciting day, and it is fun to talk about this. And what I am enjoying about the hearing is hearing my

colleagues on both sides address issues that we have both been working on, either separate at some time, then jointly.

So Gene Green and I have picked up Phil Gingrey's work and worked on the ADAPT Act. So my first question kind of deals with -- to Commissioner Gottlieb. We know the success we are having. The question is, are there additional policies that we might be able to do to even help in the guise of economic incentives that would help move on this antibiotic resistance attack and being able to get drugs quicker to the market if needed?

Dr. Gottlieb. Congressman, I would be happy to work with you on thinking through what additional steps we can take. I mean, we do have a platform now and a tail wind of some really extraordinary legislation that has just been passed in recent years. As you know, the GAIN Act did provide additional incentives through exclusivity for the development of antibiotics that were targeted to unmet medical needs. It is the kind of situations you are talking about.

And we are still in the early days of implementing LPAD and the ADAPT Act. We are going to put out guidance, as I mentioned, this summer sketching out the framework for how we intend to implement that.

And we have had multiple pre-IND meetings with sponsors. We think that this is going to grow into a robust tool for trying to get earlier, more expedited approval of drugs targeted to these special situations.

I think there are some things we can do to think about how we reimburse these kinds of products in the marketplace. So to the extent that we are asking sponsors to develop antibiotics that are going to be used on an emergency basis, or a very limited basis, a reimbursement model where you pay per use might not be the most efficient way to provide an appropriate incentive.

So we might want to think of things like site licenses. These are things that have

been considered in the past, where hospitals might pay a licensing fee for access to a drug of that kind of nature. That might provide an incentive, more of an incentive. That is obviously outside of my scope.

Mr. Shimkus. Well, let me jump in here, because one hurdle we haven't overcome, we were told earlier in the process that I have been involved with, was the issue of tradable vouchers, which I didn't get across the finish line.

So my colleagues understand that there is a need, and that may not be the venue. So I would hope we would keep thinking if there is something else that we can do that might get us to the table where we can send another signal about this. And you don't have to talk about it now. Just this is the a to raise that issue.

Let me go on the same line of questioning on antibiotic resistance and talk about just where we are on the rapid diagnostic ability, rapid diagnostic test to be able to identify quicker so that we can intervene earlier. Any comments on that?

Dr. Gottlieb. Well, I mean -- and Dr. Collins will probably opine as well -- this technology is becoming more and more available at the point of care. We used to rely on blood cultures that would take days to grow out organisms and we would just give sort of broad spectrum antibiotics until we figured out what patients were infected with and we could tailor therapy.

Now you have the ability to sequence organisms or you gain the ability to sequence them at the point of care. We are doing things with respect to next-generation sequencing, in collaboration with NIH, that I think is going to be very important to making these opportunities available.

Dr. Collins. If I may, we are running a prize competition right now. And, again, 21st Century Cures had a specific call-out to us to do prizes using the EUREKA part of the bill.

For AMR, we are basically asking competitors to come up with a means within 4 hours of being able to determine what is the infection and does it have multiple drug resistance in the case of a urinary tract infection or pneumonia or sepsis. That would be a dramatic game-changer if we had that information in that period of time. There are a lot of competitors out there. There is 20 million bucks out there for the one who wins this, 10 from NIH, 10 from BARDA. And I think that could be a pretty exciting moment if we can get the technology to that point.

Mr. Shimkus. Well, yeah. Thank you very much. And I am going to end on this, which is still a positive note.

So I am also very excited about the All of Us campaign. The University of Illinois is involved with it, and that is kind of part of my area. And so it is exciting.

And same issues. We had a telecommunications subcommittee hearing yesterday on big data, algorithms, all this stuff. Then I segued into my visit with Washington University, which is close to my home. I am in the St. Louis metropolitan area. So I know that university well, and I know the associated hospital that they work in conjunction with.

They have been so excited about the passage of the 21st Century Cures Act because in their research -- and I toured them just last week during the break and did Alzheimer's, new technologies that really drill down to the cellular structure, antibiotics, which is kind of one of the worlds in which I focus on individually.

And they just reiterated the importance of consistency. Sometimes we have been inconsistent in the funding streams, and the 21st Century Cures has established a consistent streaming and commitment to what we are doing in the health-related field. So I want to thank you, and thank you on behalf of the University of Illinois and Washington University.

Dr. Collins. If I may, in one sentence, just say thank you all for what you did in the Innovation Fund for 21st Century Cures, providing consistent support over a course of 10 years for these projects, which clearly are going to need that kind of sustained funding in order to be successful. And it is often difficult to see a path for sustained funding in the year-by-year appropriations. So thank you.

Mr. Shimkus. I am done. I yield back.

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

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

Ms. Matsui. Thank you, Mr. Chairman, for holding this hearing today and for Dr. Gottlieb and Dr. Collins to be here today as we talk about the implementation of the 21st Century Cures Act.

As we worked together on this bill, patients were always at the center of our conversations. And as we move forward, patients are still at the center as we implement this bill.

I am particularly concerned with research and drug development that affects patients with rare diseases, because for a small population of patients it is often very hard to drugs and treatments through the approval process. I just can't tell you how many individuals have come to me with their concerns, in wheelchairs, and with their stories.

Because finding cures for rare diseases is not only important to the patients with rare diseases and their families, but to all of us, because you never know where a cure is going to come from, and often research and drug development on one disease may create results for another. So we need to leverage all the tools that we have.

I would like to hear about some updates, some provisions that I worked on in Cures that were aimed at encouraging innovation for patients with rare diseases.

Sections 3012 and 3016 of the law were designed to encourage the development of targeted drugs for rare diseases, including allowing manufacturers to leverage data from previously approved applications for new indications.

We see that all of the time with rare diseases as many patients use drugs off label as their only options, drugs that were approved as safe and effective but not for their specific condition.

Dr. Gottlieb, can you provide an update on implementation of these provisions?

Dr. Gottlieb. If I may, Congresswoman, I just want to build on what you said. And I appreciate your comments and your commitment to these efforts.

To the extent there are challenges associated with the development of drugs for rare diseases, sometimes it is difficult to enroll these trials as well. We have taken steps to try to facilitate that.

I think also what we are seeing are situations where, because the biological basis is so well established for some of these drugs and we can select which patients will likely derive a clinical benefit, we are seeing clinical benefit very early in the development process.

And that was the point of trying to see how we can apply the accelerated approval mechanism to achieve what you outlined, the ability to expedite these products to the market when we do observe an extraordinary clinical response in an early stage trial, knowing we are going to be able to get the confirmatory evidence.

Building on those two provisions that you mentioned, we are going to be releasing very soon a guidance that I first announced probably 3 or 4 months ago that we were developing, which is a targeted therapies guidance. It is going to outline very specifically how sponsors can get approval for products that are targeted to biological markers rather than certain disease tissue states, if you will. So tissue-agnostic drugs.

And the best example would be a cancer that might appear in multiple organ systems but be driven by the same biological marker. If you can demonstrate that a drug targets the underlying biological mechanism, you can get approval now across all those different indications.

We are also, to the point you made, making robust use, in my opinion, especially in the oncology setting, of the provision that allows us to give supplemental indications more easily based on existing data in the public domain or references to literature rather than having to, in many cases, replicate the new clinical trials in those indications where we have a very strong biological rationale to know that the drug works there.

That was the other point of my opening testimony today, the ability to extend approvals in other settings that are proportionate to where the original approval was given. So you approve a drug in a second-line oncology situation, and then making it easier to then extend it into a frontline indication when the evidence starts to accrue.

Ms. Matsui. Well, thank you very much for that update.

Dr. Collins, how can NIH's Precision Medicine Initiative benefit rare disease patients?

Dr. Collins. Precision medicine, as a concept, is trying to get away from one-size-fits-all to identifying the individual characteristics that are going to lead to better prevention and treatment.

While the Precision Medicine Initiative flagship, called All of Us, is not particularly well designed to deal with rare diseases, because even with a million people there may be relatively few with a truly rare disease, the whole rare disease field is very attached to the precision medicine idea.

You can see what has happened with cystic fibrosis, which was mentioned earlier, where we now have therapeutics that are specific for the particular kind of misspelling

that that individual has in the cystic fibrosis gene. That is a good example. And we want to see much more of that, because there are at least 7,000 of these rare diseases for which we know the genetic mutation but we don't yet have a treatment.

We at NIH are working hard with our colleagues at FDA on something called the Therapeutics for Rare and Neglected Diseases Program, TREND, which is part of the National Center for Advancing Translational Sciences, because there are some of these disorders that are so rare that industry is not interested, at least initially, in investing in them, although there is more interest now than there used to be in industry.

And I think we are making real headway. And something that the 21st Century Cures bill did was to give TREND the ability to run phase three trials on those disorders which we did not have at NCATS before, and we are grateful for that.

Ms. Matsui. Okay. Well, thank you very much. And I yield back.

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

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

Mr. Lance. Thank you, Mr. Chairman.

And good morning to you both.

Dr. Gottlieb from Middlesex County. Is that right.

Dr. Gottlieb. That is right.

Mr. Lance. Very good.

Dr. Gottlieb, throughout the 21st Century Cures dialogue we heard about a number of innovative treatments that companies were pursuing that would target specific genetic mutations in patients with rare diseases. I am the Republican chair of the Rare Disease Caucus here in the House.

This is, of course, quite encouraging. But we have also heard that there can be

multiple genetic subtypes of each rare disease and that can further complicate drug development in clinical testing in already challenging circumstances.

To ensure that as many patients can benefit from these new technologies as possible and as quickly as possible, as you know, section 3012 authorizes the FDA to rely on data that accompany previously submitted drugs that use the same or similar technology.

Could you elaborate a little further -- and I know you have been discussing this -- about the ways in which the FDA has utilized its authority to date and what we should be doing more, perhaps, here at the congressional level?

Dr. Gottlieb. Thank you, Congressman. And the provision, I think, that you have built into 21st Century Cures that you are referencing, I think, really anticipated the future and what we are seeing.

The truth of the matter is, it is still early days in terms of the drugs that we are seeing that are targeting in many cases what are inherited disorders where you have a genetic change that drives a disorder but you have multiple subtypes that all produce the same clinical circumstance. And the question becomes, if you study one genetic subtype, when and how do you extend the approval into the genetic other subtypes without requiring the sponsor to enroll in a clinical trial in each one, especially when each one might be only a handful of patients?

We are currently having discussions with sponsors around this very principle. I think what Congress built into the law is giving us the latitude that we need to be thoughtful about how we can think about this and extend approvals across the range of subtypes that drive a common phenotype. And I think you will see us exercising that authority in some upcoming approvals. And we also plan to address this, to some extent, in the targeted therapies guidance that we will be releasing soon.

Mr. Lance. Thank you, Doctor.

And how does FDA's familiarity with an underlying technology affect subsequent product applications and the supporting data the agency expects to be included?

Dr. Gottlieb. Well, I think our ability to understand how the product works and how it intervenes in the molecular basis for a disease is what drives our ability to make these extensions that you are talking about and give us confidence that a drug that works in one setting is going to have the same clinical performance in another setting where there might be a slight genetic variation but it leads to the same phenotype. So what you reference is instrumental in our ability to make these determinations.

Mr. Lance. Thank you.

I was pleased that language was included in the bill authorizing grant funding for the study and expansion of continuous manufacturing. New Jersey has been a leader in this area, including our State university, Rutgers, and others as well, bringing together research institutions and industry to advance technology.

What steps are being taken by the FDA to carry out the language included in the act regarding what I have just discussed?

Dr. Gottlieb. This has been a very high priority for the agency trying to facilitate the development of a platform for continuous manufacturing. We are going to continue to give grants to institutions that are helping to develop the tools that are going to enable us to continue to move this forward.

We think continuous manufacturing represents the future. It is going to provide a much, much more robust way to manufacture products, especially some of the newer products that we are seeing. We think that it provides certain safeguards from potential drug shortages.

And I think it also might help us repatriate manufacturing back here to the United

States. The ability to manufacture off a small footprint that is driven by high technology lends itself to domesticating that process as opposed to outsourcing it to other countries as we have seen with traditional manufacturing. So I am hopeful that this is also going to help us build up a robust domestic industry.

Mr. Lance. Thank you. I certainly encourage repatriation. And congratulations on your appointment and your confirmation.

And, Dr. Collins, it is always a pleasure to be with you, and I look forward to being with you again at NIH, particularly on Rare Disease Day.

And, Mr. Chairman, I yield back 8 seconds.

Mr. Burgess. The chair thanks the gentleman.

The chair recognizes the gentlelady from Florida, Ms. Castor, 5 minutes for questions.

Ms. Castor. Thank you, Mr. Chairman.

Dr. Collins, the 21st Century Cures Act funded NIH to provide support for biomedical research through the NIH Innovation Fund. This focused on four vital research priorities to address some of the greatest challenges in disease prevention and treatment.

Back home in Tampa, we are home to the only NCI-designated cancer center in Florida, the Moffitt Cancer Center. And just in my short time in Congress I have been floored at the progress that we have made in treatments and cures for cancer. And yet, there is so much more to be done. And I think the Beau Biden Cancer Moonshot that is part of 21st Century Cures is an exciting research initiative because it will accelerate cancer research and improve screenings and treatments for cancer.

Can you discuss some of the research that the Beau Biden Cancer Moonshot Initiative is funding and how it may contribute to addressing the burden of cancer across

the country?

Dr. Collins. Yes, I would be happy to.

We convened a blue ribbon panel of some 28 individuals who are the most visionary folks we could identify to figure out what would be the best way to take additional resources coming forward from 21st Century Cures and do things that we otherwise wouldn't have been able to do. And they came up with a series of 10 different areas that were ripe for further investment.

And I don't have time to go through all of them. I will just mention one because it is so much on everybody's mind right now as a source of great excitement, and that is the area of cancer immunotherapy.

This, which for 40 years has been labored by a very small group of people, particularly Dr. Steven Rosenberg at the NCI, has arrived in the last few years as the most exciting development in cancer treatment in a very long time. You know, we have had surgery, we have had chemotherapy, we have had radiation, and that was sort of it.

And now we have a fourth modality, and a modality which, when it works, is capable of taking somebody with widely metastatic disease from melanoma, or somebody with advanced leukemia or lymphoma, and not just providing a response, providing what appears to be a cure. And when you see that, it is enough to make you believe that we should put every bit of energy in this to figure out how to get it to work for all cancers.

And that is what the Moonshot is making it possible for us to do. Working with industry and this partnership that we just announced a month ago, we are trying to figure out why doesn't it work when it doesn't and what could we learn from that. Why doesn't it work for pancreatic cancer? Why doesn't it work for most cases of prostate cancer or breast cancer? It seems to work for a certain subset, but the immune system

ought to be able to recognize those cancers too. What can we do to find that answer, working closely with our colleagues at FDA in this?

And you have probably heard that just in the last few months the first so-called CAR-T cell approaches to leukemia and lymphoma are being approved, which is an example of this.

So, again, thank you to the whole Congress for recognizing that this was one of those areas that was ready for a big boost. And the $300 million --

Ms. Castor. Well, I share your excitement for immunotherapy. I have heard it directly from my researchers at home and from families now, that they have additional hope in their life.

How about Alzheimer's disease? Give us the same sketch for hope and promise now under the 21st Century Cures Innovation Fund in Alzheimer's.

Dr. Collins. So 21st Century Cures funded the BRAIN Initiative, which is an incredibly ambitious effort to understand how those 86 billion neurons between your ears do what they do, and each one of them with maybe a thousand connections. And that is going to provide us with this foundation of information about neuroscience that we just have not had.

There is a huge effort, of course, more directed at Alzheimer's disease, and Congress has been increasing our funding through the regular process.

Ms. Castor. Right. There hasn't been enough in the past.

Dr. Collins. And it has been going up wonderfully well. And we are now in a position, I think, to take both the basic science coming from the BRAIN Initiative and the clinical applications that are possible through the regular appropriation and really turbo charge this effort to come up with answers.

And we need those answers, as all of us know who look at those 5 million people

who are already affected and look at what is going to happen in the next few decades with the aging of our population if we don't come up with a solution.

I am guardedly optimistic, although this is a really hard problem, that we are on the path that is going to figure out what to do to prevent this disease in those who are at high risk before it even strikes.

Ms. Castor. How can the public monitor progress here? You might go online and do a Google search, but that won't get to the heart of the matter of what is happening over the coming years because of these investments.

Dr. Collins. So we try our best through NIH to make public information available, but we don't think it is appropriate for us to be out there marketing what we do. So we are educators, but we are not necessarily doing the best job of communicating to people who are interested. We count on the media or we count on interested advocates to get the word out, particularly the Alzheimer's Association and other advocates like that.

And I do think the consciousness of the public has been raised about this. But in terms of tracking what is happening month by month, we need better opportunities to do that. I agree with you.

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

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

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

Mr. Bilirakis. Thank you, Mr. Chairman. I appreciate it.

Thank you for your testimony.

Dr. Collins, as one of the co-chairs of the Congressional Parkinson's Caucus, I was proud that we included a neurological condition surveillance system as part of Cures. It is estimated that one in six people suffer from neurological disorders. This neurological

surveillance system would gather information about patients, including incidences, prevalence, and also demographics and outcome measures.

I know that the CDC would run the surveillance program, but NIH has the experts that would use the data. How will having this information available to NIH assist biomedical research at the agency and in the research community at large?

Dr. Collins. Thank you for the question.

That feature of 21st Century Cures, which as you point out is assigned to CDC to develop this neuroscience assessment of prevalence and incidence of neurological conditions, it is certainly something that if the data were available we would find it quite useful. I think at the present time, because of the funding issues, CDC has not been able to act upon that.

We are certainly deeply invested in Parkinson's disease research, including working with industry on something called the Accelerating Medicines Partnership. It is possible that the All of Us Program that is going to enroll a million Americans over the course of the next 3 or 4 years will provide some useful information here because some of those folks are going to have Parkinson's, quite a few, in fact, when you consider how frequent the illness is and the fact we are talking about a million people.

But it won't quite substitute for what you asked CDC to do. I think this is a circumstance where the ability to get the information is not trivial. It takes a lot of resources, a lot of time. And here is where CDC, as I understand it, is having a hard time figuring out how to actually do what Cures Act asked them to do.

Mr. Bilirakis. Thank you.

Dr. Gottlieb, during my Cures roundtables in my district I heard from a woman who had a child with Duchenne Muscular Dystrophy. She talked about two hurdles: the challenge of acceptable biomarkers and the need to incorporate patient-reported

data. In Cures, we had a provision dealing with patient-reported data, as you know.

You mentioned in your testimony there is a new section on patient experience data. Can you update us on when that came online, how FDA will incorporate that data in the review process, and what does FDA hope this type of feedback will lead to?

Dr. Gottlieb. We are starting to do that right now, Congressman. Cures did give us the ability to expand on these opportunities to try to build in better measures of the patient experience as a measure of how we look at efficacy for purposes of approval.

I think the opportunities that we are going to have that I am most excited about are better opportunities to look at things like physical performance. So you talked about Duchenne Muscular Dystrophy. One of the objective endpoints that we use in measuring outcomes in that clinical setting is traditionally a walk test that is meant to approximate physical function and look at whether or not new therapies are improving physical function or slowing the rate of decline in that clinical setting.

But what if we had a tool that allowed a patient to wear a device, maybe it is a watch, that measures their physical performance in routine daily living? That might be very preferable to trying to do it in an artificial setting of a clinical trial where you are doing it in a sort of random fashion when a patient comes into a doctor's office for an evaluation or checkup. If you are able to look at a patient in their daily life, that might provide a much more objective measure of how a drug might be impacting their life.

And so these are the kinds of opportunities that I think we have with new technology. They are the kinds of opportunities that I think that this legislation is giving us the legal basis to make better use of. And this is what I am looking to the future for.

Mr. Bilirakis. Very good. Thank you.

Again, Dr. Gottlieb, the other issue that was brought up in my roundtable was the challenge of acceptable biomarkers. This has been an issue that I have brought up in

prior hearings.

Can you update us on changes FDA has made? And how can we encourage the greater use of biomarkers, particularly for rare disease patients where traditional clinical trials may be too hard for them to -- they are limited in population, as you know. So if you could answer that, I would appreciate it.

Dr. Gottlieb. Thank you, Congressman.

Here, again, Cure has provided us with new opportunities. The legislation did provide us an opportunity for the incorporation of drug development tools into our regulatory process. We have a biomarker qualification program now. We have eight biomarkers that are under consideration, all by various consortia.

We also have another program that allows us to develop sort of other kinds of measures that can measure efficacy or performance of patients in clinical settings. And we are going to qualify the first, for major depressive disorder, very soon, a new survey tool that looks at outcomes for patients who are suffering from MDD in the clinical setting. Again, this was a qualification process that was created by Cures as well.

So these are moving forward. We are seeing a lot of interest in these kinds of opportunities, and we think this is going to provide a very important framework for the future.

Mr. Bilirakis. Excellent. Thank you very much.

I yield back, Mr. Chairman.

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

The chair recognizes the gentlelady from Colorado, 5 minutes for questions, please.

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

One of the proudest achievements we had in 21st Century Cures, I thought, was

the establishment of the Oncology Center of Excellence at the FDA.

Dr. Gottlieb, as you mentioned in your testimony, this first-of-a-kind center enhances coordination between the FDA's drug device and biologic centers to leverage the agency's expertise on cancer. I am hoping that the OCE model will be a success that we can use for other diseases. Can you tell us what this center is already doing to advance the work in cancer treatment?

Dr. Gottlieb. So we have already been able to use the center to do consolidated clinical assessments on a range of products. I think the most profound sort of manifestation of the opportunity that such a center affords us is what we saw with respect to the approval of two gene therapy products targeted to some rarer cancers that I think do provide a meaningful opportunity, and perhaps a profound opportunity, for patients to get more advanced and potentially more curative therapy in settings where there wasn't very good available therapy prior to the approval of these products.

I think the essential point is that the center allows us to consolidate the clinical review and take a more multidisciplinary approach to how we look at the evaluation of efficacy and safety around these products. And we do think that this kind of center approach represents the future of how we want to approach other therapeutic spaces.

Ms. DeGette. For other diseases?

Dr. Gottlieb. Immunology, a center for neuroscience. These are things we are contemplating. Now, it is very important that we get it right in the setting of oncology since this is our test case and our first model for this.

Ms. DeGette. And can you do more if you get full funding for this center?

Dr. Gottlieb. Well, we appreciate what Congress tried to do in appropriating funds to the center through NIH. As Dr. Collins will attest, there have been some challenges associated with transferring those funds to FDA, some legal challenges.

And so we look forward to continuing to have discussions about how we could fund this. It hasn't been funded to date in part because of the challenges associated with how the money was allocated, to nobody's fault. So we do want to work on that.

Ms. DeGette. It is a frustration for us too. So if there is something we can do to help, let us know.

I just have a couple of more quick questions. I want to ask about the IRB provisions. You guys know that for about 10 years I worked on a Protection for Patients in Research Act that would streamline the IRB process, and I was really happy to get some of that signed into law as part of Cures.

I know that many of the IRB provisions in Cures have not been implemented yet, but I am hoping maybe you can talk to us about how the Cures provisions that streamline the IRB process will help reduce administrative barriers for scientific research.

And we will start with you, Dr. Collins.

Dr. Collins. Quickly, I think it has been very helpful to have those features in the Cures Act. One thing that we are now insisting upon is that multisite trials, which used to have multiple different IRBs, each of which might have some opinions about the wording of the consent form, we no longer think that that is the right way to do things. And having a single IRB for multisite trials has now become the norm. And, basically, if that is not to be the case, we need to understand why.

And your support for that has been really helpful because we generally lost many months in the process of trying to --

Ms. DeGette. We lost many months, and we lost many millions of dollars every time we did a research study.

Dr. Collins. Indeed. So this makes a lot of sense, and we appreciate the opportunities to do that.

Ms. DeGette. And sort of a related issue, and that is the clinical trials. The Cures provisions establish processes at the FDA to qualify biomarkers, incorporate patient experience and real-world evidence into trials. The committee recently built on the Cures provision in the FDA Reauthorization Act. What more can we do to improve the way and modernize the way we are doing clinical trials?

We can start with you, Dr. Gottlieb, on that one.

Dr. Gottlieb. I think that there is a lot we can do. And here again, Cures gives us a platform for doing it. And this is one place where I think that we are trying to take the spirit of what Congress did in Cures and wanted us to do and extend it.

And so we are looking at opportunities to build in more modern approaches to how we design clinical trials, more adaptive designs, seamless clinical trials, other ways to make clinical trials easier to enroll and allow us to get measures of clinical benefit earlier. There is a lot we can do, I think, to think differently about how we move away from a very old paradigm for design of clinical trials and modernize these approaches.

Ms. DeGette. So I will just ask both of you for all of these issues I am talking about. If you need additional legislative authority, please let us know so that we can work together in a bipartisan way to expand this. Because I think this is really going to help us get cures much more quickly to approval.

And thank you, Mr. Chairman. I yield back.

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

I am going to recognize myself 5 minutes for questions. I delayed at the beginning.

Let me just pick up on that point that Ms. DeGette just made. This is, of course, our first oversight hearing on the Cures bill and it is the 1-year anniversary of the House passage of the legislation, but really the lines of communication should be constantly

open.

And I would just echo what she said. If there are statutory changes that need to be made to give you the flexibility to deliver the products we want you to deliver, we would like to hear from that. Let's not wait another year to have those discussions, is all I would say.

Both of you -- and I have got several questions that I will probably submit for the record because I am going to run out of time -- but each of you mentioned a specific disease that I would like just a little bit more information.

Dr. Collins, you mentioned sepsis.

And, Dr. Gottlieb, you mentioned sickle cell.

On the issue of sepsis, you said a 4-hour diagnostic. My generation of physicians, you had to draw blood cultures so many hours apart. Two weeks later, if they grew something, great, then you isolated the bacteria. You put it on Kirby-Bauer sensitivity media. Seventy-two hours later, you would have the antibiotic to use if the patient was still with you. And you talk about a 4-hour timeframe. That is pretty incredible.

Dr. Collins. It is. And it is still not a reality, but I can tell you the competitors for this prize are coming along pretty quickly. We already narrowed it down to a manageable group that is making notable progress.

Yeah, I am in the same generation of physicians you are, Dr. Burgess, and the idea of waiting all that time. Because, of course, what did we do then? We basically had to give every imaginable possibility, cover it, with the appropriate antibiotics, which meant everybody got broad spectrum antibiotics, probably got steroids, probably got all kinds of other support without really knowing what we were doing. We were flying blind.

We want to take the blinders off and get the technology that is now capable of doing this. And much of it is based on genomics, the ability to find the DNA of that

organism and have it tell you what that organism is capable of. There is no reason we can't do that.

And yet, you are right, it took a long time to get to the point of actually talking about this as a reality. Even a few years ago most cases of sepsis were being managed pretty much like you and I did when we were residents.

Mr. Burgess. Empirically, never use one drug if three will do. Yeah, I remember those days.

Dr. Gottlieb, you mentioned sickle cell. And it wasn't really part of the Cures bill, but at one of our reauthorization hearings in this room probably a year and a half ago the statement was made it had been 40 years since the FDA had approved a new sickle cell drug.

And you talk that there is one now that is on the horizon or has it been approved? Could you elaborate on that.

Dr. Gottlieb. This is a reference, Congressman, to gene therapy. We are seeing products in development using tools of gene therapy targeting a range of blood disorders, including sickle cell disease.

Gene therapy lends itself -- I think some of the early applications of it that we are going to see are going to be what we call ex vivo applications where you take cells out of the body, you manipulate them with genes, and you reinsert them in the body.

And one of the opportunities is around the ability to do that to blood cells. And we know that if you can get sickle cell patients, patients with sickle cell disease, to express more fetal hemoglobin, you can treat the underlying disease. You don't cure it, but you effectively dramatically reduce the phenotype.

And so there are approaches like that, trying to use gene therapy to change the nature of blood cells in these patients where you take them out, you change them to

express fetal hemoglobin, and then you put them back in.

I will just close by saying these aren't going to be risk free. So it is going to be important that we carefully select the patients who are going to benefit the most from these kinds of approaches. But we are going to see these opportunities, I believe in the near future, if not in sickle cell disease, in other blood disorders.

Mr. Burgess. And, again, my point, for illustration, was the very long time horizon between the FDA's approval of the last sickle cell medication. And it is encouraging there is something on the horizon on gene therapy.

And I heard a discussion from a couple of researchers yesterday about some retinal diseases that they were targeting. And, again, this just seems like something that is tailor made for surrogate endpoints to be able to use either the perception of light, the restoration of vision, able to read a certain size print.

And it was a one-time therapy, which then gets into the whole issue, how do you price something that is only given one time? If it gives you back your sight, it is probably worth a lot as far as value to the patient.

I am sorry, Dr. Collins, you wanted to say something?

Dr. Collins. I was just going to say with regard to sickle cell, there is a protocol now in the clinical center at NIH that has treated more than a dozen patients using a gene therapy vector, and it gets better and better as they keep refining it. And there are individuals now in that protocol who have essentially normal hemoglobin values and who say they have never felt better, they are free of those horrible crises that were part of their life.

We are really making progress in this space. But it has got a ways to go to be sure that the risk -- because you have to do something to make space for the corrected cells in the bone marrow. So you have to do a limited ablation. That is not a trivial

thing to do, and we need to be sure we are getting that part right.

Mr. Burgess. Well, I appreciate the update. That is encouraging.

And I would just say, several years ago, I guess it has been over a decade ago, I had the opportunity to talk to Dr. DeBakey. We gave him a gold medal honoring him here in the House of Representatives.

And one of our discussions, he and I went down to the VA the next day, and he told me when he graduated from medical school -- and I guess it was sometime in the 1930s -- he said: I knew I wanted to go into research, I knew I wanted to be a researcher, but there was nowhere in America to go, and I had to go to Germany in order to learn how to be a researcher, to get the credential to be a researcher.

Now scientists come from all over the world to the National Institutes of Health to get the credential to be a researcher. I hope Ken Burns reflects that in his opus.

Thank you. I will yield back my time.

And who am I recognizing next?

I recognize Mr. Cardenas from California, 5 minutes for questions, please.

Mr. Cardenas. Thank you very much, Mr. Chairman, and also Ranking Member Green. Thank you so much for having this really important hearing.

Implementing 21st Century Cures, so far it appears we are doing a pretty good job of making progress. And so I want to thank you for that. And also if you could please share with your team our thanks for doing all that good work with the law that we passed here. Also, I want to thank you two gentlemen, doctors, for your service.

My first question is -- we will start with FDA -- are there any vacancies in your department?

Dr. Gottlieb. There are, Congressman. You know, we are undertaking a process to try to reform our hiring system. I think, as you know, we have had challenges

onboarding people in a timely fashion, and that has led to a backlog of vacancies that we are very focused on addressing.

Mr. Cardenas. Do vacancies in any way contribute to a slowing down of the incredibly important work and progress of saving lives?

Dr. Gottlieb. Yeah. The truth of the matter is, you can go always do more with more. It is hard for me to argue that if we are down hundreds of slots in our drug center, for example -- and I think that is what you refer to -- that that doesn't have an impact on the overall operation.

We recently launched a hiring pilot around the user fee slots, and we are going to announce very soon the results of the new hiring process that we are going to be implementing on a pilot basis that dramatically shortens the time that it will take us, we believe, to onboard a new hire. If that pilot is successful, we plan to try to roll it out on a wider basis across the agency.

Mr. Cardenas. Thank you.

And same question to NIH. Are there any vacancies in your department?

Dr. Collins. So we are fortunate in that more than 80 percent of the dollars that go to NIH go out in grants to institutions all over the country, in all 50 States. And so the work that we support largely doesn't get done within our own four walls. We do have an intramural program which is about 11 percent.

Mr. Cardenas. Do you have vacancies?

Dr. Collins. We do in that area because we are always turning over. And there was a hiring freeze at the beginning of the administration, which we are happy to say we have now come to a place where we are able, for the most critical hires, to be able to bring people on board.

Mr. Cardenas. So there is a semi-freeze still? Critical hires, you make the point,

you get to hire them, but others are still in abeyance?

Dr. Collins. We are very focused right now on ways that we might be able to improve our administrative efficiencies. So Dr. Tabak, who is my principal deputy, and I are looking at all the hires very carefully and personally to be sure that we are making the right --

Mr. Cardenas. And as well you should. I am not questioning your practices. My real question to you on that front is, what can Congress do to help you be more efficient of filling those vacancies, if there is anything that we can help in that, effecting a better, streamlined process?

Dr. Gottlieb. Cures is going to help with the resources that you provided to us to be able to go out and target hires with certain technical expertise where we have a hard time competing on a salary basis with people with extraordinary expertise. And so that is helpful to us.

I think that our challenge -- we don't have a hiring freeze in place right now, we are able to move on hires -- our bigger challenge has been the length of time it takes to onboard someone and the fact that if you are recruiting a medical reviewer who is a physician in an academic institution looking to make a career move and it takes us 12 months to bring them on, they might take another job in that interim.

And so we need to find processes that allow us to compress that timeframe. We think we have done it. I have pulled over from Cedar one of their very senior executives, an extraordinary woman who is a very senior manager, worked at NIH for a while, to head up this hiring pilot. And we are very focused on trying to make this work with respect to the PDUFA slots. And then, if we can validate our new hiring template that we will be rolling out soon to provide transparency around it, we will implement it on a wider basis.

Mr. Cardenas. Thank you.

In the interest of time, I want to get to my last question. And if you could please think of Max asking you this question and try to keep your answer short. I only have 30 seconds left.

If Max were to ask you, "Should we continue to help people become scientists and doctors and get an education?" should we continue to help them do that?

Dr. Collins. Not only should, we have to. That is the future.

Mr. Cardenas. Okay. So if Congress actually took away some of the little things that help them get their education, would that be a good thing or a bad thing?

Dr. Collins. That would not achieve the goal that we all would have to agree is critical for our future.

Mr. Cardenas. Remember, you are talking to Max. Is that a good thing or a bad thing?

Dr. Collins. It is a bad thing, Max.

Mr. Cardenas. Thank you. Thank you very much.

I yield back the balance of my time.

Mr. Guthrie. [Presiding.] The gentleman yields back.

And the gentleman from Indiana, Mr. Bucshon, is recognized for a 5 minutes for questions.

Mr. Bucshon. Thank you, Mr. Chairman.

Commissioner Gottlieb, as physicians we share a common desire to ensure patients see tangible benefits from advancements in science and medicine. The 21st Century Cures Act law laid a critical foundation to advance personalized medicine, especially as it relates to therapeutics.

One area which was not really addressed by Cures was improving the regulatory

paradigm for clinical diagnostic tests, which are often the entryway into personalized medicine. Both FDA-approved in vitro diagnostics and laboratory-developed tests have experienced incredible growth in terms of the number of tests offered in the market and the levels of their complexity. So physicians and patients rely on these tests more and more to make critical, life-altering decisions.

Unfortunately, the diagnostics regulatory framework remains outdated, inconsistent, and insufficient, leading to potential patient safety concerns and barriers to innovation, in my view. Congress needs to do more, and I applaud your recent statements that it is time for legislation in this area.

My colleague and I, Diana DeGette, released a discussion draft of the Diagnostics Accuracy and Innovation Act, DAIA, as you probably know, which aims to modernize the regulatory framework for diagnostic tests. Notably, the DAIA would create a new pathway to regulate clinical diagnostic tests outside of the medical device framework while ensuring consistent regulation regardless of the test developer.

We believe the DAIA takes the best of what the FDA, CMS, and the States have to offer and creates a new, modernized regulatory paradigm building on the expertise and capacity of these critical entities.

I am pleased that the agency, the FDA, is working now on technical assistance on the draft legislation, and I look forward to working with you and the agency to make the diagnostics reform a reality of this Congress.

So the question I have is, what is your sense of what improvements need to occur in this important area and how it relates potentially to the personalized medicine space and how Congress can be helpful?

Dr. Gottlieb. Thank you for the question, Congressman.

As you know, we for a very long period of time exercised enforcement discretion

with respect to this entire space. But I think as we see these technologies become more sophisticated and become more important to the clinical practice of medicine, and as we see some variability in the quality of the products that patients are using, on which they are making very important medical decisions, we do think there is a role for FDA to play in certain aspects of these products and across certain products.

But we also believe that the traditional medical device approval process is a poor fit for the regulation of LDTs, laboratory-developed tests. And we think that there is an opportunity, in our view, to fashion a regulatory framework through legislation that can provide a more appropriate fit to the kind of technology we are talking about here.

And so we are very eager to work with Congress on this. I think the opportunity couldn't be more ripe to do that. I think that the clinical opportunities for patients couldn't be more seductive and the need to do that.

So we will provide whatever support and technical assistance we can to Congress, including the white paper that we put out, which laid out some of our thinking on this.

Mr. Bucshon. Thank you very much. I appreciate that.

Ms. DeGette. Will the gentleman yield?

Mr. Bucshon. Yes. I will yield to Diana DeGette.

Ms. DeGette. Thank you.

So, Dr. Gottlieb, we really want to get going on this early in the new year. So the quicker we can get that technical assistance, the better.

Thanks.

Mr. Bucshon. Thank you.

This is just kind of a doctor thing. I was a doctor before. So, Dr. Collins, I am interested in, you know, the NIH many years ago, as you know, interleukin treatment, which is kind of an immunotherapy type treatment, probably maybe 25 years ago even,

especially as it relates to malignant melanoma I think --

Dr. Collins. Exactly.

Mr. Bucshon. -- the NIH pioneered a lot of that work. Now it is 20 years, 25 years later, or whenever the date is, but I remember this from my residency in medical school.

I mean, we are in an exciting time, but it has been quite a long time since immunotherapy has really been something we have been trying to develop, right? What do you think has slowed us down? I know we have gotten to a good place now, but what do you see as the barrier to actually getting us across the finish line to making this better?

Dr. Collins. Well, Dr. Bucshon, it is a good example of how you have to build over many years from basic science efforts, from a lot of failed hypotheses, ultimately building the strength to understand how the immune system can be brought to bear on cancer. And now, understanding things like checkpoint inhibitors and how you can take immune cells out of the body and take them to school and teach them what they should go and look for in that person's cancer, we know how to do that now.

I think now the big barrier is to figure out how do we take the successes with melanoma, with leukemia, with lymphoma, with some cases of lung cancer and kidney cancer, and get this to work for everything.

It should. Every cancer is making abnormal proteins, which the immune system should be able to see. But cancers are very clever in hiding that. And if we could activate in every situation -- pancreatic cancer, brain cancer, prostate cancer, breast cancer, ovarian cancer, all the places where we still don't do very well -- and get the immune system to work there, then we could really declare victory.

We have got a long way to go, but, boy, it is so different than where we were a

few years ago where we weren't sure this was ever really going to work. And now it clearly is. We just need to expand that effort. And the Moonshot is making that possible.

Mr. Bucshon. I am glad you highlighted the importance of funding basic science research and how that really over decades sometimes leads to things that you don't necessarily think it might lead to, but it gets you to a place where we are today, especially as it relates to immunotherapy.

Dr. Collins. That is a great point. Thank you.

Mr. Bucshon. Thank you. I yield back.

Mr. Guthrie. The gentleman yields back.

The gentleman from California, Ms. Eshoo, is recognized for 5 minutes for questions.

Ms. Eshoo. Thank you, Mr. Chairman.

It is wonderful to see both of you here.

And, Dr. Collins, I always like to say to my constituents that NIH stands for our National Institutes of Hope.

And I think that you have both spoken to that today with not only your opening statements, but in your answers to questions to members. So thank you for your special leadership for people in our country.

Dr. Gottlieb, in the 21st Century legislation Congresswoman Susan Brooks and myself had a bill that was included, Strengthening Public Health Emergency Response Act, and it established a priority review voucher, a PRV, to encourage the development of medical countermeasures, countermeasure drugs and vaccines at FDA.

And I know that the FDA plans to issue guidance to address this. I would like to get maybe a quick update from you on the timeline of that guidance.

Dr. Gottlieb. I appreciate the question, Congresswoman. I can get back to you specifically. I believe that that guidance is going to be out before the spring. I can give you a more specific timeframe on that.

Ms. Eshoo. Okay. That would be wonderful.

And under the current legislation, the PRV sunsets in 2023. But if a product were being developed today, many of them need more time. So 5 years would bring us to the middle of a development cycle. Are you concerned about the uncertainty that that would yield?

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[12:04 p.m.]

Dr. Gottlieb. As you know, Congresswoman, the 21st Century Cures Act also provided for GAO to undertake a more comprehensive look at the PRVs more generally, and I think we are looking forward to that evaluation to have a better sense how these are impacting development and how they are providing an incentive for sponsors to try to develop therapies against some of these unmet needs that Congress is looking to target additional incentives towards.

So we are hopeful that that will help validate some of what the early experience has been, but I think we are really looking towards that report to answer some of these questions.

Ms. Eshoo. Good. Thank you very much.

Under the original legislation, the 21st Century Cures Act, H.R. 6, that the House passed, and we are celebrating its first anniversary today, the funding was mandatory. And then the final legislation authorized the increases to FDA and NIH, but didn't appropriate funding, making it subject to the annual appropriations process.

So for all that the legislation calls for, which is obviously very important, how are both of your agencies doing with the appropriations process?

I mean, really, up front, because when the SPRO was put into this thing I just rolled my eyes, because we wouldn't have a drop of oil left in that strategic reserve if everything that claims to be funded by it were actually funded. And I understand that that is only part of it.

But how are we doing?

Dr. Collins. So my understanding is -- and, again, this was pretty complicated financial negotiation -- that the way in which this now applies is that the funds provided by 21st Century Cures do get allocated. All it requires is for the appropriators to basically --

Ms. Eshoo. I know how it works. I am just asking, is it working for you? Are you getting enough money to do what you need to do in the timeframe that you have set forward and the challenges of the legislation? I know what the process is.

Dr. Collins. Okay. I got it. I am sorry.

Ms. Eshoo. You don't need to repeat that. I already said it.

Dr. Collins. We are in fact able to utilize the funds that came forward in fiscal year 2017. We look forward --

Ms. Eshoo. Of course you can use them, that is not the point. Are you getting what you need in terms of funding for the first year of a 10-year period?

Dr. Collins. Yes, we are.

Ms. Eshoo. How about you, Dr. Gottlieb?

Dr. Gottlieb. We have been allocated the funds that we expected to date.

Ms. Eshoo. Good.

Dr. Collins. I will tell you, I ran into Chairman Cole in the hallway coming here. He wanted all of you to know that he loves the fact that you provided funds to NIH, but he wishes that somehow --

Ms. Eshoo. Well, we don't provide funds.

Dr. Collins. Well, in a way. But he wishes that somehow people who gave him his allocation would pay attention to what he needs also. I had to pass that along from Chairman Cole.

Ms. Eshoo. Well, he can talk to Members. He doesn't have to give you the

message.

I just want to add one more thing, and that is that I think not enough spotlight has been placed on this going to our future scientists and researchers, that this tax bill that is moving through the Congress in terms of graduate and postgraduate education is a killer. It is an absolute killer. So that should be part of the record.

Thank you, gentlemen, very much.

Mr. Carter. [Presiding.] The gentlelady yields back.

The gentlelady from Indiana, Mrs. Brooks, is recognized for 5 minutes for questions.

Mrs. Brooks. Thank you, Mr. Chair.

And before my colleague from Colorado has to go to another hearing probably, I just wanted to thank her and former Chairman Upton for working with both sides of the aisle to get the most important piece of legislation. I have been here 5 years. I think it is the most impactful and important piece of legislation that I have been involved in. I am very proud of it.

I also was very proud to have worked with Congresswoman Eshoo on the piece of legislation that got included in this.

I want to ask you, Dr. Gottlieb, to follow up just a little bit more, since we did get included the medical countermeasures, which just, for the record, just to make sure, these are specific material threats identified by the intelligence community as posing a material threat sufficient to affect national security or that has been determined to seriously threaten national health security.

And there is no commercial market for this. This is why we had this limited priority review voucher. And it is seen as our private sector partners' very real incentive to continue to develop critical vaccines, whether it is things like Ebola or Anthrax or other

types of threats.

Now, since we have gotten this passed, has the FDA seen an increase or a renewed interest from the private sector partners in engaging with the FDA in the medical countermeasure space?

Dr. Gottlieb. I would have to get back to you with the specifics, Congresswoman. I know we have had some engagement with sponsors. I would have to get back do you to let you know how far along that engagement is. We have had pre-IND and some discussions with sponsors, I am aware of that.

Mrs. Brooks. We would welcome you getting back with us because that is what the point of it was, was trying to make sure that the private sector had the incentives in which to engage, and we need to know what is working and what is not working.

You also in your written testimony talked about the FDA's emergency use authorization, the 2017 guidance extending authorities to be applicable to animal drugs. Can you share any updates or any hurdles the FDA has faced or potential challenges in implementing this emergency use authority?

Dr. Gottlieb. The EUA authority now out now applies to animal drugs, as you have said. I would have to get back to you, again, in terms of where we are talking to sponsors. I am not aware of the interactions that we have had to date. But we see this as a big opportunity to potentially give EUA to drugs targeted to animals where if you had a pandemic, for example, where the infection was transmissible to the animal and they can become a vector, you want to be able to treat the animal as well in the kind of a setting.

Mrs. Brooks. Thank you for explaining that so well because that is so very important. We focus on people, but because animals can transmit so many diseases, I think that is critically important.

Dr. Collins, in my time remaining, can you talk with us a little bit more with respect to the Precision Medicine Initiative, the focus on the All of Us Research Program. And I understand when I was in another hearing you might have spoken about it already a bit. But obviously this large group of volunteers from around the country that are going to be providing genetic data, biological samples, and so forth, a new growing field.

What are some of the challenges you are seeing or what are your hopes for this All of Us Research Program? Can you talk about it a bit further?

Dr. Collins. My hopes are that with a million participants this is going to be the most significant study ever undertaken to identify what the factors are that allow people to stay healthy, because many of these participants will be healthy, and if illness happens, what is the best way to manage it.

So we will have such an enormous database. It will be accessible, with all the personal identifiers removed, to researchers who have qualified ideas to try the learn from it.

It will also be a platform where many clinical trials can also get started because these participants will have been preconsented for contact to see if they would be interested in taking part in a clinical trial, say, for diabetes or Alzheimer's risks. So that should greatly speed up the ability of doing all kinds of research that now is slow and expensive.

But I think most of all, to be part of this, these millions folks are going to teach us things about health in America that we just didn't know and how we can move from the one-size-fits-all approach, which is kind what we are stuck with most of medicine, into something that is much more individualized, the precision medicine idea.

It will take a while for this to build up its strength in terms of what it is going to teach us about medicine. But over the course of the coming years, I don't think very

many things will happen in terms of understanding health without somebody pointing out what all of us told us because of the size and scale of that effort.

Mrs. Brooks. You have contracted or you are entering into partnerships, if I am not mistaken, with hospitals, various community health centers, I assume --

Dr. Collins. Yes.

Mrs. Brooks. -- the VA, to be a part of this.

Dr. Collins. All of those.

Mrs. Brooks. Will the other researchers that might not be affiliated with those institutions have access as well?

Dr. Collins. Absolutely. Anybody who is qualified to be able to put forward a hypothesis that is scientifically reasonable will have access. We are not trying to limit this at all. The joy that I hope will come out of this is these discoveries which will come from people who maybe didn't even know they were interested in this but had a great idea.

Mrs. Brooks. And how will people be recruited to be participants?

Dr. Collins. So those who are currently covered by health provider organizations that have signed on to be our partners will be approached. But anybody in the United States will be able to join.

When we launch this next spring, you will see a lot about this. We hope all the Members of Congress will decide to join. It will simply mean getting on the Internet, reading some material, deciding about a consent, giving a blood sample, and doing a very simple physical exam.

Mrs. Brooks. Thank you very much. Thanks for your work.

I yield back.

Mr. Carter. The gentlelady yields back.

The gentleman from New York, Mr. Engel, is recognized for 5 minutes for questions.

Mr. Engel. Thank you very much.

And let me say, I have long been a committed advocate for those suffering from rare diseases in their families. I was the author of the ALS Registry Act and the two most recent Muscular Dystrophy CARE Act reauthorizations.

And the work has shown me how great the need is for new therapies and just how much hope and comfort medical breakthroughs can bring to patients and their families. And that is why I was pleased to support the passage and contribute to the 21st Century Cures Act.

So thank you to both doctors for being here today and for helping us carry this important work forward.

Let me ask both of you this question. I feel that there should be formalized, straightforward ways to gauge the safety and efficacy of medical treatments, and that is why I worked to ensure that language on biomarkers was included in the 21st Century Cures. These tools are valuable. They tell us the state of a person's health. It can help make these kinds of evaluations better.

I was happy to work with Congresswoman McMorris Rodgers to include provisions on biomarker development qualification. I know that the FDA regularly employs biomarkers during the drug approval process, but there has not been a formal procedure in place for biomarker development and use.

My understanding is that a lack of taxonomy and evidentiary standards has made it difficult to develop workable biomarkers that can be replicated during the drug approval process.

So I am wondering if each of you would talk a bit more about how NIH and FDA

will work with each other, industry, academia, and other stakeholders, to develop better biomarkers and improve the way they are used for clinical trials and drug approvals.

Dr. Collins. I will start. Congressman, I appreciate the question because that is something of intense interest for both of our agencies.

For several years we have run something called the Biomarkers Consortium, which is a joint NIH/FDA/industry effort to try to identify opportunities where biomarkers that seem to be potentially valuable in terms of predicting response to therapy can be validated, and there has been a lot of activity in that space.

More recently, take an example of cancer, this new Partnership for Accelerating Cancer Therapies, PACT, has as its main goal identifying biomarkers for cancer immunotherapy that could be folded into the way in which we make selections about which clinical applications are going to work.

We worked with the FDA a year or so ago also to develop a biomarkers glossary so that we could all really agree about what the terminology means. You mentioned that taxonomy can sometimes be a little tangled up. So we have an agreed-upon way of using the language and the terminology.

But I will turn it over to my colleague, because obviously this is critical for figuring out how best we can come to approve therapies.

Dr. Gottlieb. I will just add briefly, Congressman, I think this is another place where Cures and the provisions that you worked on, you talked about, have given us important new tools to create a framework that is going to lead to more development of these kinds of biomarkers.

To give you some sense of what we have already achieved, we have entered into or received 11 letters of intent around the qualification of biomarkers through the provisions that you crafted for the development of drug development tools and have

engaged with 10 external sponsors already around the development of these biomarkers.

And we have even more engagement with especially the development of clinical outcomes assessment tools also, which are another element that have become critically important to try to foster more efficient drug development.

So that might not sound like a big number. In our estimation it is a profound number given the fact that these are still early days in the development of these new frameworks and we are seeing this level of interest.

Mr. Engel. Thank you. Thank you both.

Dr. Gottlieb, I want to focus on biomarkers. So let me ask you this question. With respect to the section of 21st Century Cures on qualification of drug development tools like biomarkers, the proposed FDA workplan for 21st Century Cures Act Innovation Account activities says: Once fully implemented, this section has the potential to transform drug development and review.

Could you expand on that, please? And how do you think that drug development tools like biomarkers will affect patients on the real world level? And how soon will we see these effects?

Dr. Gottlieb. Well, one of the challenges in the past was that when we had validated tools that were used to help make drug development itself more efficient, in many cases those tools were validated in the context of a single clinical trial, and that clinical trial was the intellectual property of a single sponsor. They didn't become tools that were in the public domain that could be easily used by other sponsors who could then piggyback on these kinds of opportunities to use biomarkers as a way to facilitate more efficient development.

I think what Congress foresaw in the development of this new framework was the ability to have consortia and other entities, academic institutions, others, develop

biomarkers that can become part of the public domain and become tools that many sponsors could use in an efficient fashion to help make their development programs more efficient.

So we are very helpful that this new framework, which it is an entirely new paradigm and way of thinking about the development of biomarkers as drug development tools, is going to lead to a lot of new opportunities.

Mr. Engel. Well, I want to thank both of you for excellent testimony and also for excellent work. Thank you so much.

Thank you, Mr. Chairman.

Mr. Carter. The gentleman yields back. Now the chair will recognize himself for 5 minutes for questions.

Let me begin by thanking both of you for being here and both of you for the important work that you do.

Dr. Gottlieb, I will start with you. I wanted to ask you about the executive order that was signed by President Trump the beginning this year that had to do with the one-in, two-out rule of regulations that were being imposed by the agencies, a rule, by the way, that I very much support and am very happy that he put into place.

But I was just wondering, has this really impacted you in any way in trying to implement care or cures?

Dr. Gottlieb. Not in a negative fashion, Congressman. We have periodically over the course of the history of the agency taken opportunities to do periodic looks at our regulations to make sure that they are not outdated, that they are still having their intended purpose. And I think that the executive order provides us another good basis to do that, and that is an important exercise.

We have certainly been able to find places where there are regulations that are

outdated or maybe no longer relevant that we think perhaps we could repeal in its entirety. I mentioned a couple of times we have a regulation defining standards of identity for the baking of cherry pies. We have one such regulation on the books.

But keep in mind that the executive order applies to regulations that are imposing new regulatory burdens. Many of our regulations are deregulatory. In many cases we are promulgating regulations that are actually saving money and making the process itself more efficient.

So we have been able to operate very efficiently under that framework, and he we think it is a constructive framework.

Mr. Carter. Great.

Dr. Gottlieb, you and I have spoken many times. As you know, currently I am the only pharmacist serving in Congress. And of importance to me and all of my colleagues, of course, is the opioid epidemic in our country.

One of the things that I have pushed as a pharmacist has been the fact that in my mind there is a gap, if you will, I refer to it as a gap, between what physicians can prescribe for pain, that being Tylenol, Acetaminophen, Tramadol, if you will, and then you go to the opioids. And I refer to that as the big gap there.

Now, once you get past perhaps Lyrica and Neurontin, you really don't have any other choice but to go to the opioids. And as part of Cures and as part of CARA, you have been given the authority in the FDA of streamlining, of fast-tracking some of these nonaddictive treatments.

First of all, have you gotten from the pharmaceutical manufacturers any applications for these type of drugs? And have you done anything to implement this?

Dr. Gottlieb. We are seeing the development of what you would refer to as nonaddictive opioids, drugs that maybe hit the same receptor but through a different

pathway and might not have the same addictive qualities. I mean, it still needs to be demonstrated through rigorous science whether in fact that is going to hold true.

But we are seeing the development of these kinds of products. As you know, some of them are in early stages of development. Such products would qualify potentially for all the opportunities for expedited review, including breakthrough therapy status, and that would be something that would be confidential, however, unless the sponsor chose to disclose it.

I would also pull into the discussion the development of medical devices, because we talk about systemic therapy for the treatment of pain in many situations where the pain itself is very localized. And there is a way to, through a more sophisticated device, deliver anesthesia locally. You can potentially prevent the application of systemic therapy.

And so we are seeing those opportunities as well, and we are going to be taking steps in the near future to try to incentivize those kinds of opportunities.

Mr. Carter. And you of course understand how imminent this problem is and how we need help. So I suspect this will be on the top of your to-do list.

Dr. Gottlieb. It is on the top of my to-do list.

Mr. Carter. Dr. Collins, I suspect NIH is very much involved in this in collaboration as well. I know that your Partnership for Accelerating Cancer Therapies is something that you have been working on to address really the cancer problem, but my hope is that this is something that you will duplicate, if you will, to deal with the opioid problem as well.

Dr. Collins. And we are in fact deeply engaged in that, Congressman. We will in fact on December 12th and 13th hold a meeting of 33 pharmaceutical company representative, NIH and FDA, building on studies that we have carried out over the last

few months to really put in place a framework for a public-private partnership that has never been tried before, to do exactly what you are talking about, to develop these nonaddictive but highly potent pain medicines, which we desperately need.

I will just point out this morning in the New England Journal there are two publications on the development of monoclonal antibodies against something called CGRP that are showing great benefit for migraine for people who have been resistant. It is a good example of a nonaddictive kind of pain medicine working on a very different pathway than opioids.

We have a lot of basic science we can build on now to do that, but we need the full partnership of industry as well, and I think everybody is ready to do that.

Mr. Carter. There is no question in my mind about it. As I have said, over my years of practice in pharmacy I have seen nothing short of miracles come out from the research and development from the pharmaceutical manufacturers. They need to step up now and they really need to help us with this problem. This is a national epidemic, and I am very confident that if they set their minds to it, they can do just that.

Dr. Collins. They are ready to do just that. It has been really quite exciting working with companies over the course of the last 6 or 7 months to see just how ready they are to roll up their sleeves and put their time and resources into this problem.

Mr. Carter. Absolutely. And I appreciate you, both of you, and your cooperation in assisting them and fast-tracking this as much as we can.

Okay. The chair now recognizes the gentleman from Missouri, Mr. Long, for 5 minutes for questions.

Mr. Long. Is that because I am the only one left?

Mr. Carter. Yes, sir.

Mr. Long. Thank you, Mr. Chairman.

I want to say, kind of reiterate what my friend Susan Brooks here, Congresswoman Brooks next to me said earlier. And that is, when people ask me, "What is your biggest accomplishment in Congress? What are you the most proud of?" just 21st Century Cures, period, case closed.

And that was done in a huge bipartisan fashion. As Chairman Upton mentioned earlier, 51 to nothing out of this committee, which you never see. And there were a lot of people that had a big part in that, such as Diana DeGette and Chairman Upton.

And I would be remiss without mentioning my buddy, Super Max, right here on the front row, who was a big reason that we got that through, and he attended a lot of hearings.

And, thank you, Super Max.

But we do a lot of things in a partisan fashion here in Washington, unfortunately, I think, most of the time. But one thing that we did do in a bipartisan fashion was 21st Century Cures.

And, also, there were a lot of folks that when they looked out at a hearing here in the 115th Congress and were looking at the Director of the National Institutes of Health, a lot of us got together from both sides of the aisle and said we would like to see you sitting there again. And so that came to fruition also.

So it is an honor to have both of you gentlemen here today. It truly, truly is.

Dr. Gottlieb, I am going to ask you a couple of questions here. 21st Century Cures included a provision to facilitate better dissemination of healthcare economic information, and in January the FDA published draft guidelines on this issue.

Could you discuss any feedback FDA has received from stakeholders? And what do you think is working well? And are there any ways you think that communication could be improved?

Dr. Gottlieb. Thank you for the question, Congressman.

I think this is a very important provision of Cures. I think to the extent that we can facilitate a more seamless exchange of information between product manufacturers and payers, we can incentivize the development of different kinds of contracting arrangements that maybe could allow products to be priced more closely to value.

I think this is an important element of trying to make sure we have a competitive market for how products get priced in the market. So I think that this is important to clarify what FDA's role is and isn't in regulating this information.

You are right, we received a lot of questions with respect to the draft guidances that were put out almost a year ago. We are going to be finalizing those guidances in the very near future. I said before the end of this year earlier, we might slip slightly into the new year in terms of when we get out those final guidances.

But our aim will be to go beyond what we did in the draft guidances to try to create a framework that provides for the free exchange of this kind of information and articulates, as Congress intended, that FDA doesn't intend to play a role in regulating the exchange of useful information in this context, even if it might have some authority to do that.

Mr. Long. You note in your testimony that the use of real world evidence could help streamline clinical development and could help inform the safe and effective use of medical products. Could you speak to the FDA's efforts to incorporate real world evidence into regulatory decisionmaking?

Dr. Gottlieb. We are already seeing those efforts come to fruition, in part owing to the authorities and the nudge that we got from Congress that you wanted us to make more widespread use of this evidence, especially as the tools for collecting this evidence and drawing conclusions on the basis of it got more sophisticated.

We recently approved a supplemental indication on a heart valve based entirely on real world evidence gathered from a patient registry. And we have also granted supplemental indications to some drugs in part on the basis of data that was derived from real world evidence -- or real world evidence that was derived from real world data, excuse me.

So this is becoming a part of the regulatory process. I think where it is going to have even more prominent application is in the post-market setting where we are opening up a framework for sponsors to be able to satisfy their post-market requirements on the basis of real world data or real world evidence collected from real world data.

Mr. Long. Okay. Thank you.

And I noted earlier that -- of course things pop into my mind that don't pop into other people's mind -- but when you were talking about gene therapy, just as you said that, Gene Green walked in.

So I think it is a different gene therapy, unless you want to tell us something, Gene.

I yield back.

Mr. Carter. The gentleman yields.

The chair recognizes the gentlelady from Indiana, Mrs. Brooks.

Mrs. Brooks. Thank you for allowing me to speak out of order, Mr. Chairman.

My good friend and colleague from Missouri, Mr. Long, besides acknowledging that it was awesome to have Max and his mom here, and I want to thank him, but I also want to acknowledge that a Hoosier family has also been here, Laura McLinn and her son Jordan, who is back in the office.

He suffers from Duchenne Muscular Dystrophy, and they have also been active in Indiana in advocating for Cures. And I just wanted the folks who are testifying and who

are devoting their lives to know that this matters to so many families. And I just wanted to acknowledge them for being as here as well.

Thank you. I yield back.

Mr. Carter. The gentlelady yields back.

Seeing there are no further members wishing to ask questions, I would like to thank all of our witnesses again for being here today.

I would like to submit a statement from the Healthcare Leadership Council for the record.

[The information follows:]

******** COMMITTEE INSERT ********

Mr. Carter. And pursuant to committee rules, I remind members that they have 10 business days to submit additional questions for the record. And I ask that witnesses submit their response within 10 business days upon receipt of the questions.

Without objection, this subcommittee is adjourned.

[Whereupon, at 12:31 p.m., the subcommittee was adjourned.]