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21ST CENTURY CURES: INCORPORATING THE PATIENT PERSPECTIVE

FRIDAY, JULY 11, 2014

House of Representatives,
Subcommittee on Health,
Committee on Energy and Commerce,
Washington, D.C.

The subcommittee met, pursuant to call, at 9:00 a.m., in Room 2322, Rayburn House Office Building, Hon. Joseph R. Pitts [chairman of the subcommittee] presiding.

Present: Representatives Pitts, Burgess, Shimkus, Murphy, Blackburn, Gingrey, Lance, Cassidy, Guthrie, Griffith, Bilirakis, Ellmers, Upton (ex officio), Pallone, Engel, Capps, Schakowsky, Green, Barrow, Castor, Sarbanes, and Waxman (ex officio).

Also present: Representative DeGette.

Staff Present: Clay Alspach, Chief Counsel, Health; Gary Andres,

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Staff Director; Mike Bloomquist, General Counsel; Sean Bonyun, Communications Director; Leighton Brown, Press Assistant; Paul Edattel, Professional Staff Member, Health; Brad Grantz, Policy Coordinator, O&I; Sydne Harwick, Legislative Clerk; Robert Horne, Professional Staff Member, Health; Carly McWilliams, Professional Staff Member, Health; Macey Sevcik, Press Assistant; Heidi Stirrup, Health Policy Coordinator; John Stone, Counsel, Health; Jean Woodrow, Director, Information Technology; Ziky Ababiya, Minority Staff Assistant; Eric Flamm, Minority FDA Detailee; Karen Lightfoot, Minority Communications Director and Senior Policy Advisor; and Rachel Sher, Minority Senior Counsel.

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Mr. Pitts. Subcommittee will come to order. We are going to have early votes, so we are going to have to start. We understand the minority members are on their way.

The chair will recognize himself for an opening statement. Today's hearing provides us with an opportunity to examine perhaps one of the most important aspects of the 21st Century Cures initiative. What does medical innovation or faster cures mean for patients? Keeping our work centered on the patient and understanding the patient perspective will bring much needed focus on results for patients who may lack adequate treatment options. Remember, there are only effective treatments for 500 of the 7,000 known diseases impacting patients today.

While FDA has developed an enhanced structured approach to benefit risk assessment in regulatory decisionmaking for human drug device and biologic products, the committee recognizes the value of considering patients in decisionmaking about therapy development and access. Assessment of a drug or device's benefits and risk includes an analysis of the severity of the condition treated and the current treatment options available, and getting the patient's unique perspective should be a part of that assessment.

One of our witnesses today, Pat Furlong of the Parent Project Muscular Dystrophy, PPMD -- and I must say Pat is accompanied by Mary Bono Mack, a distinguished former member of this committee. Welcome,

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Mary. And Pat will explain how this organization was founded to create opportunities for families waiting for therapies to stop Duchenne muscular dystrophy from claiming young lives. To quote Pat Furlong, quote, "Patient-focused drug development acknowledges the need to gather input from patients and their caregivers to create a more complete assessment of the benefit-risk equation, encouraging predictability, and increased flexibility within the review process. The clock is ticking for patients who need and deserve access to promising therapies," end quote.

I would like to applaud her tireless work drafting guidance PPMD recently released that actually quantifies patient priorities and preferences. This guidance will serve the Duchenne community and every other patient community because it provides a path for other patient groups to follow. This was an enormous undertaking, and I am confident it will make a substantial contribution to the entire medical community.

I would like to welcome our witnesses today and look forward to learning more about the assessment of benefits and risks central to medical product development, regulations, and healthcare decisionmaking and the tradeoffs between desired benefits and tolerable risk. Thank you.

Any member on the majority side seeking recognition?

Chair recognizes the vice chairman, Dr. Burgess for the remainder

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of time.

[The prepared statement of Mr. Pitts follows:]

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Dr. Burgess. And thank you, Mr. Chairman.

And Dr. Woodcock, thank you for joining us again. It is always good to see you, always good to have you as a witness. You always provide valuable testimony, and our second panel representatives. I also want to acknowledge just as the chairman did, many of the patient organizations that you represent have worked well with our office and myself over the last several years.

Mr. Chairman, the laudable goals of the 21st Century Cures initiatives, and they are indeed are laudable, but we got to remember, at the end of the day, it is all about patients. Doctors want to heal. We want to cure. That is why we entered the profession. No doctor ever wants to tell a patient there is nothing more we can do. The good news is that the golden age of medicine is really right around the corner. The doctors of tomorrow will have tools at their disposal unlike any before in human history. The ability of tomorrow's doctor to alleviate human suffering is going to be unparalleled and unmatched in history. Yet every day that goes by where these tools are not realized is a day that patients and their families have to struggle through the pain and suffering of their condition.

Every day counts for these Americans and for their families. For those who struggle with rare diseases, their struggle is only compounded by the lack of biomedical research. For those patients, it is difficult to see over the horizon. We have much work to do on

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this committee, and we have done a lot in the past. We particularly celebrate the 2-year anniversary of the Food and Drug Reauthorization Act that was just a few days ago. That was a good template. It was a good method for moving forward, and I appreciate that the Cures initiative is following that template, but there is no doubt that we can do much more.

I welcome the testimony of our witnesses, and I will yield back my time.

Mr. Pitts. The chair thanks the gentleman.

[The prepared statement of Dr. Burgess follows:]

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Mr. Pitts. And now recognize the ranking member of the full committee, Mr. Waxman, 5 minutes for opening statement.

Mr. Waxman. Thank you very much, Mr. Chairman.

This hearing is a fitting followup to Wednesday's hearing on clinical trials. After all, it is patients who live with the diseases and conditions for which treatments are being sought, and this hearing, which is called "21st Century Cures: Incorporating the Patient Perspective," illustrates that we should take every opportunity to understand their experience.

Congress has a long history of listening to concerns of patients. That is what I did in 1983 when I wrote the Orphan Drug Act. That law came up when I heard from a constituent, Adam Seligman, who had a rare disease called Tourette's Syndrome. Adam was forced to take a drug that he could only get from Canada because, at that time, there were no effective treatments available in the United States. When his drugs were seized at the border, his mother made a desperate call to my office begging me to do something.

I set out to figure out why there were no drugs in the U.S. for Adam's condition. We discovered that Adam was not alone. There are 134 drugs for rare diseases but only 10 had come to market solely as a result of industry. We knew we had a problem on our hands, and we set out to solve it.

The Orphan Drug Act has been a resounding success. Today, there

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are over 400 drugs for rare diseases, and I want to welcome the National Organization for Rare Diseases here today and look forward to their testimony.

I am telling this story about the Orphan Drug Act not only as an example of how Congress has listened to the concerns of patients and acted on them, I tell it because it is an example of appropriate use of legislation. In the case of rare diseases in the early 1980s, there were very -- there was very clear evidence of a market failure in need of congressional action.

In the context of the 21st Century Cures initiative, we need to assure that both FDA and the drug and device companies are listening to the concerns of the patients. FDA has a long history of engaging with patients, both in the context of advisory committees and in its review of drugs and devices. In the 2012 FDA Safety and Innovation Act, Congress pushed FDA to do even more to hear patients' concerns, and I look forward to hearing more from FDA today.

From what I can tell, the agency has taken that mandate seriously and is engaged extensively with the patient community. We should ask today whether FDA has adequate resources to continue to do this work.

As I mentioned on Wednesday when we had our last hearing, when it comes to legislating in complicated scientific areas, like the conduct of clinical trials, we need to proceed with great caution. For example, one issue in the area of clinical trials that is likely to

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come up today is how to incorporate so-called patient reported outcomes. As I understand it, this is an area that is multifaceted and scientifically complex. Congress should ensure that FDA has the flexibility and authority to make use of these outcomes but not dictate how and when that occurs.

I hope FDA will tell us about how it is applying other novel approaches to clinical trials in their regulation of drugs and devices. I would also like to know whether the agency believes it has the authorities necessary to adopt new approaches and whether other new statutory powers are necessary.

Mr. Chairman, thank you for holding this hearing. I look forward to the witnesses' testimony. I must say in advance that there is another subcommittee scheduled at the very same time as this one, so I will try to be back and forth to participate in both of them.

Thank you, and yield back my time.

Mr. Pitts. The chair thanks the gentleman.

[The prepared statement of Mr. Waxman follows:]

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Mr. Pitts. Now recognize the chairman of the full committee, Mr. Upton, 5 minutes for opening statement.

The Chairman. I yield back my time. I will just submit my record -- my statement in order to --

[The prepared statement of The Chairman follows:]

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Mr. Pitts. The chair thanks the gentleman.

We have two panels today.

On our first panel, we have Dr. Janet Woodcock, director, Center for Drug Evaluation and Research, U.S. Food and Drug Administration.

Thank you for coming again today. And you will have 5 minutes to summarize your testimony. Written testimony will be placed in the record.

So, at this time, the chair recognizes Dr. Woodcock 5 minutes for opening statement.

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STATEMENT OF JANET WOODCOCK, M.D., DIRECTOR, CENTER FOR DRUG EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION

Dr. Woodcock. Thank you. We are here to discuss how drug development better meets the needs of patients. Decades ago, healthcare was very physician-centric and actually very paternalistic. We all recognize that today. It was kind of "The doctor knows best; don't ask any questions," right.

Today, the model is collaboration between the patient and the healthcare team. These changes, though, have evolved slowly in our society, and the thinking and drug development has slowly changed in parallel.

The FDA Safety and Innovation Act of 2 years ago took significant steps in this direction of patient-centric development. It contained agreements under PDUFA that FDA would sponsor at least 20 patient-focused disease-focused meetings over 5 years. Eight of these meetings have been held to date, and they have been very impactful. The first one we held on chronic fatigue syndrome, we have issued a draft guidance on drug development in this area of very serious unmet medical need. Also, under PDUFA, were agreements to advance the development and use of patient-reported outcome measures. These are measures that the patient can fill out to say from their point of view

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how well they are feeling, how well the treatment is working, what adverse events they are experiencing.

We are having an expert meeting next week and will continue to work in collaboration consortiums to try and advance the science of patient reported outcomes. This is very important to really scientifically incorporate the patient's perspective into clinical trials.

Additionally, under FDASIA, FDA was to advance the development and use of a structured benefit risk framework in drug approval decision, and this work is under way, and it really explicitly provides for considering the burden of disease, the impact of current therapies, both for good and for ill, and the tolerance of risk from the patient's point of view, and this is an extremely important set of factors that need to go into the benefit-risk decision, but we need to do this in a scientific manner and a structured manner and we are rolling out the structured benefit risk framework.

Now, for people, we know that for people with very serious diseases who may lack good therapy or actually lack any therapy, access to new treatments is their number one priority, and that is why expediting drug development programs in these areas is so important. If you look at the diagram that we have here that was provided, these data and the diagram were actually developed by the Pharma organization, talks about, shows the drug development process, and it

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is starting on the left, it shows you start with many thousands of compounds, up to 10,000 compounds at one end, the beginning, and after 9 to 13 years, you may end up with one safe and effective drug on the market.

The clinical development phase, which is the gray phase, the middle phase on this diagram, is the longest and by far the most expensive phase.

In contrast, the FDA review phase, of which much attention has been paid to, is actually the very small slice there, the white slice toward the end of the process, right before the drug gets on the market and is typically at this time less than a year in duration.

So FDA has made strenuous efforts, really, to help reform and modernize the clinical development phase of drug development because that is the major bottleneck. Not only is it expensive and long, many products fail in this phase, and there is a tremendous opportunity cost there where other treatments could have been developed.

Now, the FDASIA included several innovations to this process and the most striking being the breakthrough therapy designation program, so if we could have the next diagram. Thank you. This was mandated by Congress and was specifically directed at that clinical development phase, so that we could help when therapies were particularly promising and were designated, we could help move them through that phase more quickly. The BT designation has been enthusiastically subscribed.

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We have had over 160 requests in the 2 years since the legislation was passed. We have actually -- and this is the really surprising part, we have granted 52 designations. So what Dr. Burgess said about we are on the verge of a new era in therapeutics, I think, is reflected by this. We would not have seen this a decade ago, and we have approved six products, four new products and two new indications.

Now, it is too early to judge really the impact of the breakthrough designation program; is it really going to be able to speed up drug development? However, I will say the four products we approved, their clinical development time was 4.5 years, so much shorter than what I showed in the earlier diagram.

Also, in FDASIA were clarifications of the application accelerated approval, and we issued a final expedited draft guidance in May that includes, in response to stakeholders' requests, examples of rare diseases and includes more information on the use in rare disease. However, it is clear much more needs to be done to modernize the clinical trial process. That is the big bottleneck now in getting discoveries to patients. This can't be done, though, by FDA alone. We don't execute this process. All the stakeholders need to participate, and I think the series of hearings that have been held and the 21st Century initiative can help provide the framework for significant reform in this process.

Mr. Pitts. The chair thanks the gentlelady.

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[The prepared statement of Dr. Woodcock follows:]

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Mr. Pitts. I will begin the questioning, recognize myself 5 minutes for that purpose.

Dr. Woodcock, what is FDA's plan to advance biomarkers and the use of patient reported outcomes data during the drug development process and post-market setting?

Dr. Woodcock. Many years ago, a decade ago, we recognized that there was no structured scientific process to provide the evidentiary basis for use of a biomarker in decisionmaking, and so doctors and biomedical researchers would float new biomarkers, but there was no rigorous process by which they could be evaluated to see if they were really useful. So we actually established a process for this. It is not really in our mission, but we established it, and it is called the Biomarker Qualification Process. And we also work with the European medicine agencies and the Japanese regulators so that this would be a worldwide activity. And consortia can come into the FDA and propose a biomarker, a new biomarker, and we give them advice on what needs to be done, and then -- and also for patient-reported outcomes. And if, in fact, that evidence is developed, then we will publish a letter that is public, and so will the EMA if they accept it and so forth, and then any developer can use that biomarker or measure in a development program and will rely on it for the context of use.

We have 79 projects by different consortia in different phases of this process right now.

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Mr. Pitts. Good. Describe your plans for implementation of the structured benefit-risk framework you mentioned that -- transparent to the public and the sponsor so that the assessment of data from clinicals trials and other studies by FDA reviewers can be better understood and acted upon.

Dr. Woodcock. Yeah. Well, this is an iterative process. We have had public meetings. Then we went back, and we are piloting this in multiple -- in the different drug review divisions and having the medical officers work through this framework that we have developed and see what the results are. Then when we have that, those results, we will go back through a public discussion and talk about how -- get input on how this can be improved, so this is not something that can happen overnight.

It is a scientific process, and actually, we feel that we have -- we don't have the tools right now. They exist out in society in science, but we haven't applied them, these rigorous analytical tools to the benefit-risk decision, and so we have had workshops on this, various scientists come in and advise us, so we will have a public process once we have gathered more experience.

Mr. Pitts. I have been hearing a lot about FDA's efforts to improve the quality of pharmaceutical manufacturing. Where do U.S. drug manufacturers currently stand when it comes to producing quality medicines? Can you tell me a little bit about your plans in this area?

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Dr. Woodcock. Well, I think the major problem here is that many of our essential drugs are made -- not made in the United States, and they are made all around the world, and sometimes they may only come from a single source, and this is, I think, a real vulnerability to medicine. And in addition, we used to be a manufacturing powerhouse in drug manufacturing, but those jobs have moved offshore. And I think now we have an opportunity, with new modern manufacturing methods, such as continuous manufacturing, to actually build a high-tech industry in the United States that actually will make the drugs we need here in this country. And FDA has been collaborating with the -- this community, manufacturing community, to help bring this about, and we are very interested in seeing this happen.

Mr. Pitts. Now, we have recently heard a lot about Lung-MAP, the Lung Cancer Master Protocol trial. There are other examples of similar innovative trial designs, like I-SPY for breast cancer. What else needs to happen before these types of trials are no longer front-page stories?

Dr. Woodcock. That is a good question. We also have been advocating for this for many years, and it is wonderful to see it start to become a reality. The concept, I think, in drug development needs to be turned on its head in clinical drug development, and instead of, for each investigational drug, there is a whole clinical trial program developed with different clinical trials that take a very long time,

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as you heard on Wednesday, to get started and so forth, that there are networks that are available that investigational drugs can be plugged into. This will provide independence of an assessment but also really decrease the time and expense of assessing whether these drugs are safe and effective.

But what needs to happen, I think, is we need to expand this to more diseases. The NIH is very interested in antimicrobials in setting up a network, and other groups are looking into this, and I think you may hear today from some patient groups say Cystic Fibrosis has really successfully set up the infrastructure to have cystic fibrosis drugs rapidly evaluated once they reach the clinic.

Mr. Pitts. The chair thanks the gentlelady.

Now recognizes the ranking member of the subcommittee, Mr. Pallone, 5 minutes for questions.

Mr. Pallone. I am going to have to -- since I just got here.

Mr. Pitts. Okay. You want to yield to Green?

Mr. Pallone. Yeah.

Mr. Pitts. All right. Mr. Green.

Mr. Green. Thank you, Mr. Chairman.

Dr. Woodcock, welcome back. I want to thank our chairman, ranking member, and Dr. Woodcock for testifying. In a time where revolutionary science and technological development, we have an opportunity to target specific patient populations, advance

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personalized medicine, and transform how we approach the prevention and treatment of disease, one of the goals I think is particularly worthy of exploration is the idea of personalized medicine, in which a patient may be able to receive more tailored drugs and treatment suited to his or her specific condition.

Our understanding is the human genome is the key to that goal. Academics and researchers tell me, another piece is the potential for researchers and developers to discuss these drug and device innovations with patients during the development phase.

Dr. Woodcock, can you give us your views on the upsides and downsides of any increasing permissibility of communication between patients and developers during the clinical trial phase of development?

Dr. Woodcock. It is a very interesting question. We have seen from the 1990s, where only 5 percent of drugs were targeted; in 2013, 45 percent of the drugs we approved were targeted in some way. There are barriers to locating patients and joining up patients who have specific conditions, subsets with appropriate investigational therapy, and these diseases are fragmented into smaller and smaller subsets. It is harder and harder to find these people who might be eligible for a given therapy.

The Lung-MAP trial is one way of doing that where it has multiple investigational arms in one trial, so people can come in, and they can be spread out. But there is great interest, of course, with more

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patient activism in using social media and other ways to actually match up the right patients with the right investigational drugs, and I think this is one of the challenges right now of the clinical enterprise.

Mr. Green. Well, increasing patient involvement in FDA's decisionmaking surrounding drugs, devices is a significant yet challenging endeavor. Can you provide your suggestions on how mechanisms need to be developed to accurately measure what meaningful outcomes for patients are, both in the clinical outcomes and the quality of life? Is there -- can we do that?

Dr. Woodcock. Yes. That is what I was referring to with Chairman Pitts is that there is a science of measurement, and patient-reported outcomes is one science. How do you measure how a patient feels from their point of view? And there are ways to do this, but these measurements have to be developed. We approved many drugs based on their impact on quality of life, so that is completely possible, but what needs to be done is this science needs to be developed, and we are participating in that. As I said, we have an expert meeting next week on patient-reported outcomes.

Mr. Green. Well, and the patient involvement process has to be data driven and improve the overall efficiency of drug development and maintain FDA standards of safety and effectiveness. How can Congress support the FDA in incorporating patient perspectives and regulatory decisionmaking in a way that helps deliver that innovative, safe, and

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effective medicines to the patients sooner?

Dr. Woodcock. Well --

Mr. Green. Do you need statutory authority, or do you think you already have it?

Dr. Woodcock. To my knowledge, we have the authority to do this, and I think you will hear from the next panel, for example, how patient groups can develop draft guidance, submit it to the FDA. They can run processes that actually incorporate all their points of view and those of the expert scientists, so more of that needs to be done, but I don't know that it needs more statutory authority.

Mr. Green. Can you do it within current resources, because again, you are specializing, instead of a broad brush -- and I assume it costs more when you do an individual.

Dr. Woodcock. Yes. Well, when you have 7,000 diseases that need good treatments and most of them don't have them, it would be very difficult for FDA alone to develop the standards for patient reported outcomes in each one of those diseases, much less the clinical outcomes. So much more participation of the medical and patient community is needed in drug development, and we need to find better ways to do that, but I am not sure that is through legislation.

Mr. Green. Okay. And without a doubt, our greater resources, but again, our committee has worked over the years to try and provide those resources --

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Dr. Woodcock. Yes.

Mr. Green. -- to the FDA and look forward to working with you.
Thank you, Mr. Chairman. I yield back.

Dr. Burgess. [Presiding.] The gentleman yields back.

I recognize myself for 5 minutes for the purposes of question.

Dr. Woodcock, again, good to see you, good to have you back in the committee. So you have talked about how the FDA routinely works with sponsors to apply flexibility, including the use of biomarkers, surrogate endpoints, and nontraditional trial designs, and other available tools to expedite the development of products to treat both common and rare diseases.

With respect to the common diseases, how is the FDA working with sponsors to apply these innovative development and review methods?

Dr. Woodcock. Well, for example, hypertension is a common disease. We approve drugs for hypertension based on a surrogate measure, blood pressure, that is very well accepted, and for a number of years ago, we looked at automated blood pressure monitoring, okay, and we decided it was unbiased, and so we decided that you really didn't need a control group in the same way that you would for most other diseases because you have an unbiased measure, and so we issued new approaches to studying, you know, hypertensive medicines. So that is an example.

Dr. Burgess. What could happen so that the FDA could use this

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more frequently?

Dr. Woodcock. Well, 45 percent of the drugs that we approved over the last several years use a surrogate endpoint. So we do use that when it is appropriate and it is available. What -- for many diseases, we don't know what the right surrogate is, and that is why many of the accelerated approvals have been confined say to cancer and HIV is because the science, a great deal of science has been driven in those conditions, and we understand the biomarkers. But for other diseases, there needs to be more scientific development, and that is why we are using this, for example, biomarker qualification process to try and get more biomarkers developed that we can use, but we can't just dream them up and use them.

Dr. Burgess. I thought that was your job. Well, let me ask you this. Are there situations where a majority of the scientific or research community believes that a certain biomarker sufficiently predicts the clinical outcome, but the FDA has yet to accept that?

Dr. Woodcock. There may be. I think there is a lot of controversy around use of these. You heard some of that on Wednesday. There are two sides to this. If you rely upon a surrogate, often, especially when it isn't well validated, there is more uncertainty about whether or not the drug is actually going to work or not, and so there are different points of view. And as we have all been saying, the community, the patient community really ought to have -- and

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treating community ought to have a lot of input into how much uncertainty should be tolerated, given the circumstances of that disease.

So there is -- there are situations where there is disagreement amongst various parties, external and internal, about the use of a surrogate.

Dr. Burgess. Are there any -- are you able to give us any examples of that, of a surrogate that the FDA may not right now be willing to accept?

Dr. Woodcock. Well, for example, raising good cholesterol, all right. We had a series of trials on that. Everybody thought raising good cholesterol would be really good, and in fact, it turned out to be either neutral, or in one case, it actually increased mortality, so we no longer accept that surrogate. That is the kind of example where -- and there are many others like that.

In bone density, you know, for osteoporosis, estrogens do a very good job and they decrease fractures. Although they have other liabilities. But some other agents were tried, and actually, they increase bone density, but they also increased fractures, and so we have to be careful when we use these surrogates to make sure that we are getting the intended results, clinical results.

Dr. Burgess. Thank you for that.

Let me ask you a question that is a follow up from when we visited

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in April.

Do you have an update on the status of the FDA's guidance on biosimilars naming and when that guidance will become final?

Dr. Woodcock. Well, I certainly would like to get that guidance out as soon as possible. We are working diligently on that, and I don't have any further update.

Dr. Burgess. But that was submitted as a question in April, and we are awaiting an answer.

Now, also, along with that, I asked if anyone in the administration, outside of the FDA, had provided the agency with suggestions or recommendations with respect to this guidance.

Can you, if the answer to that is yes, can you provide us with the name or names of those individuals?

Dr. Woodcock. We would have to get back to you on that.

Dr. Burgess. And again, we anxiously await your answer.

My time is expired.

I will recognize the gentleman from New Jersey, the ranking member, 5 minutes for questions.

Mr. Pallone. Thank you.

Mr. Chairman, you asked a lot of my questions, so I am going to have to move on to other things.

But Dr. Woodcock, we heard a lot at Wednesday's hearing about the accelerated approval program at FDA, and as you know, the program allows

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for earlier approval of drugs that treat serious conditions and fill an unmet medical need, and the drugs are approved on the basis of surrogate endpoints which we also learned about on Wednesday, and of course, a critical requirement of the system is that companies conduct studies to confirm the clinical benefits suggested by the surrogate endpoint, and these studies are called phase 4 confirmatory trials. So a critical part -- I want to ask about the phase 4 trials. What challenges has FDA faced with respect to phase 4 trials? Do sponsors complete in a timely manner?

Dr. Woodcock. Well, it is sometimes difficult to complete these trials, and the reason is that if you had a serious and life-threatening disease and we approved a treatment for it, you probably would be somewhat reluctant to enter a trial where you had a maybe 50 percent chance of not getting the treatment. So what we often do is ask that trials be conducted in a different stage of disease or something where it actually hasn't been studied yet, so then we can get the results since that might take time.

So I think in the early years of the program, we didn't track this as well as we should, and we did have a lot of trouble getting these trials completed. But in the current era, we are on top of this, and generally speaking, the sponsors are diligent in trying to get them completed, generally, but they have difficulty sometimes enrolling patients in these trials.

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Mr. Pallone. Another important component of the program is that when the surrogate endpoints do not ultimately show the anticipated clinical benefit, FDA could be faced with needing to remove the indication or take the drug off the market, and I imagine that is also no easy task.

Can you describe what is involved with removing the indication or taking a drug off the market and what challenges does the FDA face there?

Dr. Woodcock. Yeah. We -- generally, if the confirmatory trial failed to show benefit, the first thing we ask is the sponsor to voluntarily withdraw the drug or the indication from the market. It is only if the sponsor does not agree to do that, then we go into a long administrative process, which includes hearings and findings -- formal findings and so forth, and this can take a long time if the sponsor can test our finding that the drug isn't effective.

Mr. Pallone. Now, just a couple of years ago, we included some provisions to improve upon the accelerated approval program, and the FDA Safety Innovation Act of 2012. For example, the law made it clear that FDA could rely upon evidence developed using biomarkers or other scientific methods or tools when assessing surrogate endpoints. Can you describe what impact those legislative changes had on the program, and are there any other changes that you feel are necessary to allow you to make full use of the most recent scientific developments with

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respect to surrogate endpoints?

Dr. Woodcock. I think the legislation was very helpful. We have taken it quite seriously. We have issued guidance, final guidance on expedited programs, and probably the biggest change in the -- that the legislation brought about was its focus on intermediate clinical endpoints, and we had to have quite an internal discussion about what that means, and I think you will see us approving more products under accelerated approval based on these intermediate clinical endpoints.

Mr. Pallone. All right. Well, thanks.

Again, it is clear to me that this is an extremely complicated area and one that is not necessarily conducive to further legislation, but I wanted to ask last about the master protocol.

At the hearing on Wednesday, some panelists described some of the inefficiencies that exist in the way that clinical trials are currently conducted, and one of the suggestions for addressing those inefficiencies is to create a master protocol. So I just wanted to ask, first, can you tell us more about this, what is a master protocol? How would it help to improve the way we conduct clinicals trials? Has FDA been involved in the development of a master protocol, and are there particular diseases that the master protocol is more appropriate for than others, and if so, which ones, and are there other areas where it might be expanded?

Dr. Woodcock. Well, master protocol is one version of using

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clinical trial networks or standing clinical trials to evaluate investigational therapies where the drug development program isn't just for one therapy. It is for any therapy for that disease. So master protocol, though, has to be somewhat disease specific. You can't just have a general overall master protocol, right. It has to be focused on one disease.

For example, the one, the Lung-MAP trial is on squamous cell cancer of the lung that is advanced and -- but five different agents right now are being studied all at once within that protocol, and that is a huge efficiency. But there are other versions of standing trials or trial networks that also could be used in other diseases. And as I said, the Cystic Fibrosis Foundation has a kind of network of clinical excellence where they actually sequenced the genome of all their patients, and so they are ready when a targeted therapy comes along. They are ready. They can put those patients into the protocol, and that tremendously improves the efficiency.

So there is a -- it is a long conversation that probably can't be had in 5 minutes, but I have long advanced this concept and tried to push this concept because the current clinical trial paradigm is not sustainable.

Mr. Pallone. All right. Thank you very much.

Thank you.

Dr. Burgess. The gentleman's time is expired.

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The chair recognizes the gentleman from Pennsylvania, Dr. Murphy, 5 minutes for questions, please.

Mr. Murphy. Thank you.

And good morning, Doctor. It is always good to have you here.

Let me start out by asking about it is important for the medications and research to advance those but also for those that are already approved, and so let me ask you, we had passed the PDUFA laws awhile ago, certainly -- Mr. Griffith, you just moved between me and -- that -- that helped -- was supposed to help us get more generic drugs in the queue, but what has happened is we got 1.5 billion authorized over 5 years, but what has happened is approval times have gone up, and there are fewer approvals, even though the law was supposed to reduce all those.

Can you give me some indication of what is going on and what FDA is going to do about that?

Dr. Woodcock. Certainly. We are well aware of these issues. In June, we received 625, I believe, generic drug applications, so it is -- the rate of submission is well above what was projected in the negotiations that we held.

However, on October 1, the deadlines kick in for -- for timelines for review of generic drugs, and we are fully prepared to meet those -- those timelines as well as deal with this large backlog of pending.

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We had to hire a large number of people and totally revise our processes, reorganize the generic drug review offices and conduct many other changes, and that is what we have done over the past 2 years in preparation for the deadlines coming into effect on October 1.

Mr. Murphy. Thank you. Another question here about some labeling issues. The abbreviated new drug application that would allow generic manufacturers -- this a proposal for FDA to change a label without FDA's prior approval but then come back later on, and the FDA itself has recognized, and say, quote, "consistent labeling will assure physicians help professionals and consumers that a generic drug is as safe and effective as its brand name counterpart," unquote. But there is a concern out there that allowing these changes take place and then go backfill them later on can cause a lot of confusion in studies that have asked pharmacists and physicians this, so I am wondering where this issue stands in clarifying this.

Dr. Woodcock. Well, we have received comments on the proposed rule. It was a proposed rule, and we received many comments. We are analyzing the comments, and subsequent to that, we will have to go forward with a, you know, rulemaking process.

The proposed rule contemplated that we would actually have less disparities of labels in the marketplace on this because of this proposal because we would put up a Web site, and we would also require conformance of labels, which we cannot carry through right now, given

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the current systems.

Mr. Murphy. The committee -- we have -- a lot of us back in January asked to meet with Commissioner Hamburg and others about this, and I am not sure those things have taken place yet, so I hope this gets expedited and that these issues are addressed because I think it still leads to some confusion. So I am not clear yet in understanding even why this proposed rule was set up there to allow this individuals to change the label and then come back later and ask permission.

Dr. Woodcock. Well, currently, generic labels do not always match the innovator and they do not change their label in a timely manner, and so there will be labels out there for quite a bit of time, even with serious safety issues like new box warnings that don't conform to the innovator label, so we are trying to address this situation. And also, as generics are now 85 percent of all drugs dispensed to consumers, we are -- that they should have the opportunity, since their drugs are the ones that are -- people are being exposed to, to submit their findings of adverse events and suggest label changes, proposed label changes and actually execute them.

Mr. Murphy. Well, just hope that you will meet with the committee staff members and the companies to help clarify this because it still is not clear to me why this would be allowed, and I think it would be -- end up confusing.

I want to bring up one last thing just while you are here. I had

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sent a letter a few weeks ago to Dr. Hamburg. I am sure you didn't see this, but one of the things that is out there, too, is complications that are oftentimes reported in the media about caffeine, whether it is -- and sometimes toxic levels people take.

Dr. Woodcock. Yes.

Mr. Murphy. Through over-the-counter things, pure caffeine or some of these supplements out there for athletes, et cetera, and yet it is also in everything from chocolate to coffee and other things we promote all the time, so I am hoping, at some point, FDA can also give some recommendations in terms of individual levels per drink, per dose, per day, per male, female, the genders, for weight, age, whatever that is.

Dr. Woodcock. Uh-huh.

Mr. Murphy. Because it is still pretty confusing, whether -- whatever those products are that they can be beneficial, but I hope you will expedite that.

Dr. Woodcock. Thank you.

Mr. Murphy. Thank you.

I yield back.

Dr. Burgess. The gentleman's time is expired.

The chair recognizes the gentlelady from California, Mrs. Capps for 5 minutes for questions, please.

Mrs. Capps. Thank you for holding this hearing to our chairman

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and ranking member.

Thank you, Dr. Woodcock, for your testimony.

This is an issue very dear to me, and as you know, I am incredibly concerned about our Nation's history of excluding minority groups, especially women, from all levels of medical research, from the lab rats to the most advanced clinical trials. And reports have shown that even when these groups are included in trials, there are often too few participants in the groups to analyze the effects on them or the analyses are simply not run or reported.

I am sure you are familiar with the case of Ambien, commonly prescribed medication that recently had its label changed because it metabolizes differently in women than men, meaning that women had been receiving an inappropriately high dose of this drug for over 20 years.

In addition, in spring, a report entitled "Sex-Specific Medical Research Why Women's Health Can't Wait" was released, which provides evidence for the further inclusion of sex and gender in scientific research. And the FDA's own August 2013 report, which was initiated by the inclusion of My Heart for Women Act in the FDASIA legislation, showed that there is still much work to be done to make sure that women are fully represented in clinical trials and that the safety and effectiveness of the information is readily available.

I know the FDA is continuing to work on an action plan to address these disparities, so Dr. Woodcock, can you give us an update on where

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the agency is on this?

Dr. Woodcock. Certainly. I would expect that that would be released, you know, we would be timely in its release. I believe there was a statutory deadline or not, or there is some expectation, so we are -- yeah, we are working diligently on the action plan, yes.

But I will say for drug development, which is what we are discussing -- or I am discussing here, that we did a study, for example, in 2000 -- of the 2010, the class of 2010, the product that we approved, we found that 45 percent -- more than 45 percent of -- about 45 percent of the participants were male, all right.

So -- and we found that almost all the submissions included the required gender analysis, which has been required for drugs for 20 years, because I oversaw that when I first joined the Center for Drugs in 1994. So, it is by regulation, so we do have these, but I think the transparency of the information is the problem, and we are working on that, and we have -- I really am committed to making that information more transparent so people understand what we know and what we don't know.

Mrs. Capps. I think that to be -- I think you put your finger on something, and I want to highlight a bipartisan letter I led signed by the women of the House of Representatives urging this agency to plan -- to include clear and actionable strategies. And I think what you said about transparency and the reporting, you know, in there, in

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the action plan is a way to address this issue once and for all.

At Wednesday's hearing this week, I also asked the panel about the tools FDA is developing that could supplement our knowledge base, especially in the light of less robust clinical trial designs. The FDA Sentinel system, which I understand is making progress, if not, if slowly, to conduct post-market passage surveillance of drugs and devices, could help spot issues like adverse drug interactions more quickly. I believe the Sentinel program holds great promise, and that is why I worked to get assurance -- the Sentinel Assurance for Effective Devices Act included in FDASIA to continue progress on the program and ensure the design for both drugs and devices. Could you update us on the development of the Sentinel program, please, and what other resources or authorities do you need to get the system up and running to protect consumers more effectively and expeditiously.

Dr. Woodcock. Well, I think use of electronic health data, which is rapidly becoming available, and the electronic health records and so forth, has tremendous promise for actually finding out what happens in the real world for medical products, both that are approved recently and those that have been on the market a long time, and that is what the Sentinel system is intended to do.

We have run a mini-Sentinel network for 5 years, and that was between drugs and biologics. We paid for that out of our money that we have, and we are recompeting that to put up the Sentinel system,

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so that contract proposal is out on the street, and we hope to establish the real Sentinel system, which will be a large-scale system for surveillance.

Now, as far as medical devices, we require a unique identifier or some kind of identifier in the medical record electronically so that we are able to capture that because the Sentinel system uses those electronic records to get the information, and I will repeat for everyone that it does not take any personnel information and move it to some central database. It strictly runs those analyses within the healthcare system and then the results only are combined.

So that has tremendous promise. We feel very good about that. We actually are piloting running active surveillance on there, so when we approve a drug and we have a question about it, we can watch over time and see what actually happens. So it has -- and as more and more people get on electronic health records, we can really have more insight in what is happening.

So that is where we are with that, and it is resource limited. I have to pull resources from other activities to fund that, but I believe very strongly that this is the future.

Mrs. Capps. Thank you. I appreciate that.

Mr. Pitts. [Presiding.] The chair thanks the gentlelady.

Now recognizes the gentleman from Georgia, Dr. Gingrey, 5 minutes for questions.

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Dr. Gingrey. Mr. Chairman, thank you.

Dr. Woodcock, thank you for appearing. It is always good to see you.

I understand that a number of the challenges that have led to the duration and cost of conducting clinical trials in the U.S. to increase essentially are outside of FDA's purview. That being said, clinical trials are conducted to generate evidence used in the application for FDA approval, so how early -- my question is -- my first question, how early do you typically communicate with these companies, pharmaceutical companies, to discuss their trial design before the investigational new drug application is submitted?

Dr. Woodcock. Well, we have agreements under PDUFA, that prescription drug user fee program, and for novel products or novel indications, say they are testing a disease that really doesn't have any treatment, companies can come in and have a pre-IND meeting. That meeting is before they start their clinical trials, their first in human studies, and we talk about that development program so they can start thinking about how that is going to be done.

We do have information, it is preliminary, but looking at our information, it seems that companies that have more interactions with the FDA are able to get their products through more quickly, through the entire clinical trial process than companies that haven't had interaction with the FDA during the development process. But there

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are formal meetings that are held at different times under the user fee program, and those minutes are tracked, and we track the meetings and so forth, so there is quite a process for interaction during drug development.

Dr. Gingrey. So, you, as a manager, would be, maybe at that particular time, you make sure that your reviewers are not requesting overly burdensome data that really is not necessary so that the process can be speeded up?

Dr. Woodcock. Well, there is always a push and pull. You know, scientists of all stripes always want more data, and that is scientists in the companies and scientists in the FDA, and so we have to walk that path between, you know, getting more data and actually the cost that is generated. And we have made a number of efforts under the CITI collaboration that we do with Duke University and many, many, many other partners to try and figure out how to streamline clinical trials as far as data collection, for example. But it is -- it is difficult.

We have 1,600 meetings a year under the PDUFA, and when we have -- when we meet with companies, the supervisors are there, the senior medical officials are also at these meetings.

Dr. Gingrey. Well, that is the whole purpose of 21st Century Cures, of course, and as we get to the second panel and we hear about the associations and from the families, I am sure they are going to talk about how we can speed this process up.

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Let me -- the last question. At our first 21st Century Cures hearing, we heard that only 19 drugs, outside of cancer and HIV space, have been approved by the accelerated approval pathway since 1992, and I understand that you wrote a blog post after that hearing about how a number of drugs that were being considered under accelerated approval ultimately received traditional approval, so these statistics, according to your blog, were somewhat misleading. Can you provide some examples of when that occurred as well as the process involved?

Dr. Woodcock. Certainly. Well, for some -- for certain rare diseases, we may decide, for example, that the surrogate is fine, okay, and it correlates with clinical benefit. Then the term "accelerated approval" is a little misleading. It sounds like it is faster than regular approval, but actually, if we approve -- we give regular approval on a surrogate, it is just as fast as accelerated approval, but you don't have to do confirmatory studies afterward because we already believe the surrogate.

So, for a lot of, say, rare deficiency diseases, okay, where there is something missing, you may be able to show that you actually, when you replace that protein in the body, you give the activity back to the person, right, and so you may not have to show clinical outcomes. It is still a surrogate, but we feel it is good enough because we understand the problem that something is missing, and you deliver an active drug to the site of action of where the problem is, and that

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would be enough.

So, in many cases, we are able to do accelerate -- do traditional approval with the surrogate; that means that the patients and the sponsor don't have to go through all these confirmatory trials. I described the difficulties of that when you have a serious disease; you have approved a drug; and then you ask people to be randomized after approval.

Dr. Gingrey. Dr. Woodcock, thank you.

And my time is expired. Mr. Chairman, thank you, and I yield back.

Mr. Pitts. The chair thanks the gentleman.

I recognize the gentlelady from Florida, Ms. Castor, 5 minutes for questions.

Ms. Castor. Well, thank you very much.

Thank you, Dr. Woodcock, for everything you are doing to ensure safe and effective drugs are available for the American public and those with health challenges.

Patient -- this is a hearing about the patient -- patient involvement in FDA drug approvals, and I think we can agree, they deserve a seat at the table when companies are developing drugs and medical devices within the clinical trial process. I have long been a supporter of the Department of Defense's Congressionally Directed Medical Research Programs known as the CDMRP. CDMRP funds

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peer-reviewed research into breast cancer, autism, ovarian cancer, prostate cancer, and other diseases. And since 1993, the patients have been involved and have been a part of CDMRP, and they have a consumer reviewer as part of a peer-review panel to represent the stakeholder community, and it has been very successful in combining patient perspectives and needs with scientific research and bringing those perspectives together.

Has FDA, as you begin to consider improving patient involvement, have you looked at CDMRP to see if there is anything you can borrow from that in the drug approval process?

Dr. Woodcock. We have not, and that is a good suggestion, so we would be happy to do that.

Ms. Castor. Okay. You mentioned previously that the Patient-Focused Drug Development Initiative that was included in PDUFA was designed to hear --to allow FDA to hear from patients on how a disease impacts their life, and I understand you are scheduled to hold 20 public hearings. Share with us who FDA has met with so far. Have you started those hearings, and what -- if so, what have you learned already?

Dr. Woodcock. Well, we have learned the devastating impact, I think, of the diseases, of these different diseases on people's lives it just incredible. We had one on chronic fatigue syndrome -- that was our first one -- HIV, lung cancer, narcolepsy, sickle-cell disease,

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fibromyalgia, pulmonary arterial hypertension, and inborn errors of metabolism, and we plan to have 16 of these meetings completed by the end of 2015, but we recognize this is just a drop in the bucket of what people suffer from.

So what we are trying to do is really model how people can do this, and hopefully, it could be done more -- not put on by the FDA but by the patient groups themselves in the medical community that serves them so that they can assemble more of this information and kind of multiply the effect of this, and we are already seeing some of that. NORD, for example, has offered to help with rare diseases, for example, to have more input that way because we -- our resources are limited. We are not going to be able to cover all the different diseases.

Ms. Castor. Good. So I expect we will hear from the patient organizations later this -- later today on -- and their view on how they can be helpful and we can be effective.

I think the wave of the future really is the information we will be able to gather through the electronic health record, so it is interesting to hear what you have done already with the Sentinel initiative. I heard from research institutes back home that are doing so much in genomics and personalized medicine that they think these larger networks are the wave of the future. You say you don't need legislation, additional legislation to continue, but you are having to borrow resources from this and that.

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Dr. Woodcock. Uh-huh.

Ms. Castor. So is your advice to the committee that we need to do more in technology when it comes to improving timelines on clinical trials by focussing on these networks and the electronic health record?

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[10:06 a.m.]

Dr. Woodcock. The networks also have much -- the electronic networks have much promise in doing clinical trials.

If we could move clinical trials more out into the community and have people out in the community, like cancer patients -- most cancer patients in the U.S. who have diseases that are untreatable are not -- don't get into trials because they are being treated at places that aren't running trials. So we need to move this out into the community, make those folks eligible.

And I am on the Steering Committee of the Lung-MAP trial, and I really urged that we make sure that we are out there in the community so that anyone who has lung cancer has an opportunity to participate in this research and perhaps have a more effective therapy.

So I think the electronic health records, that is a huge different area that we are working on in how to do clinical trials utilizing that infrastructure that is going to -- is emerging.

Ms. Castor. Great. Thank you very much.

Mr. Pitts. Chair thanks the gentlelady.

Now recognize the gentleman from New Jersey, Mr. Lance, 5 minutes for questions.

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Mr. Lance. Thank you very much, Mr. Chairman.

A portion of your testimony has focused on the FDA's efforts on patient engagement. It is my understanding that ClinicalTrials.gov was intended to be a resource that provides clinical study information for patients, for healthcare providers, and for researchers. But it seems to me that the site lacks considerable information and has proven to be difficult to navigate.

Dr. Woodcock, would you please comment on the current utility of the ClinicalTrials.gov.

Dr. Woodcock. Well, I think that it has provided, along with the requirement of the medical editors of the journals that things be registered before they are going to be published -- provided tremendously more transparency into what clinical trials are ongoing in the United States.

And that has been a big achievement. All right? So we know, you know, the issue of publication bias and everything is minimized because we know what trials have been done.

However, I agree that, certainly for patients, I think that initiation of trials and understanding where there might be a trial that might be ongoing that might be available to them has also been effective, although, as you said, there are technological issues that remain. So it has made tremendous progress in transparency.

Mr. Lance. Is there a way that you and we can work together to

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improve it? And I am not suggesting that you are in any way responsible for the challenges that remain. But moving forward for the better health of the American people, how together can we improve it?

Dr. Woodcock. Well, the FDA Amendment Act required that regulations be issued around the results --

Mr. Lance. Yes.

Dr. Woodcock. -- section of this and that they consider whether to require the submission of clinical trial results for unapproved products, because much of the lag in getting results in there is that the products still are not on the market.

So NIH is the lead for this rulemaking and I think they would be in the best position, and, also, they operate the infrastructure for this database.

Mr. Lance. Thank you.

In another area, in the past several hearings, we have discussed the difficulty of various institutions communicating one with another and a lack of coordination often leads to inefficiencies.

What methods are currently in place to reduce redundancies in clinical trials? And what steps can we take together to ensure that we are not doubling up on research or making the same mistakes over and over?

Dr. Woodcock. Hopefully, most things would eventually come out and be published. But certainly in the drug development area, there

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is interest in more sharing of earlier data and sharing of failures.

But this has proven to be very a intractable area --

Mr. Lance. Yes.

Dr. Woodcock. -- for transparency. All right?

Mr. Lance. Yes.

Dr. Woodcock. But we have continued to work on that.

Mr. Lance. Yes.

Dr. Woodcock. As far as some of the things that were referred to in the prior hearing, which I was able to listen to some of, they were talking about some of the inefficiencies, say, of IRBs, where multiple IRBs -- you might have to have 100 IRBs that looked at --

Mr. Lance. Yes.

Dr. Woodcock. And I believe that there are efforts to try and address this. It is not an FDA issue. But, really, we came out a number of years ago in saying that central IRBs would really be preferable in these large multi-center trials.

And then the contractual agreements that take so long to set up with each specific site is something that has been taken on. They have tried to develop model agreements and so forth.

But that is something that the standing trial addresses because you sign this contractual agreement once and then you can do multiple investigational agents.

Mr. Lance. Are we moving in the direction of central IRBs, in

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your judgment?

Dr. Woodcock. Yes. I mean, there is certainly a consensus, I think, in the clinical trial investigator community that that is desirable, but various universities, naturally, are concerned -- legally concerned about their own --

Mr. Lance. Of course.

Dr. Woodcock. -- liabilities and so forth. And so there is a push and pull about that.

Mr. Lance. I think this is an area that we should engage in further investigation to make sure that we move forward in a manner that does not result in redundancies.

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

Mr. Pitts. Chair thanks the gentleman.

Now recognize the gentlelady from Illinois, Ms. Schakowsky, for 5 minutes for questions.

Ms. Schakowsky. Thank you, Mr. Chairman.

Thank you, Dr. Woodcock. I think you are really an excellent witness. I appreciate your answers.

Dr. Woodcock. Thank you.

Ms. Schakowsky. I wanted to go a little bit further on the problem that Congresswoman Capps raised about the underrepresentation of women.

I know you said that you found that, actually, women were

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overrepresented, but recently the Congressional Caucus for Women's Issues sponsored a meeting with leading women heart experts -- both clinical and research experts, physicians.

Those experts raised concerns that the lack of representation from women in clinical trials is limiting our ability to effectively treat women with heart disease. They were focusing in on heart disease.

And according to those experts, for the last 50 years, women's heart treatment has largely been based on medical research about men.

And even today, despite that fact, what they said is that women make up more than 50 percent of the U.S. population, that women comprise only 24 percent of participants in all heart-related studies.

And, additionally, scientists from the Women's Health Research Institute at Northwestern -- that is in my district -- have raised concerns about the disproportionate number of adverse drug effects that occur in women due to the lack of sex-based clinical research.

And, as you know, the biological, physiological, hormonal differences in males and females impact the rate of drug absorption, distribution, metabolism, elimination and, ultimately, affect the drug's effectiveness.

According to those experts, the lack of requirement for drug manufacturers to take this into account and document any sex variability early in the drug development pipeline before a drug has

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been released places consumers, especially female patients, at an increased risk of adverse drug effects.

So I want you to respond that.

Dr. Woodcock. Certainly.

Ms. Schakowsky. Many of us were really left with a very disturbing feeling because heart disease is the major killer of women right now.

Dr. Woodcock. Right. Well, I think we have to -- what are the facts on the ground. All right? One of the reasons for the disparities that they are mentioning is actually the fact that men suffer heart disease earlier in life than women.

Ms. Schakowsky. Although, let me just point out, they also said that the growing number, even though it is lower --

Dr. Woodcock. Yes.

Ms. Schakowsky. -- is younger women getting heart attacks and heart diseases.

Dr. Woodcock. Yes. Yes. So that the reason for maybe maldistribution in the trials is because there is an age cutoff, and there always has been.

In our survey, we found that there were -- 19 percent of the people in the trial in these 147 studies we looked at were over 65, which is more than in the general population, obviously, but it is -- of sick people, that is still low representation -- right? -- to save

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people with heart disease.

Generally speaking, there is often a cutoff -- age 75 -- and we are trying to eliminate those cutoffs for age and concomitant conditions so that the population will be more representative.

But to your -- could I -- to your original point, we require -- we have always required male and female animals in the toxicology studies. All right? We require what we call population -- PD -- pharmacokinetics, PK/PD, early in drug development.

And we look at -- our clinical pharmacologist look at blood levels and exposure in men and women and we understand that, usually, and that is modern drug development.

So there are multiple trials that are done that look at exposures, in other words, achieve blood level by gender and other factors, liver failure, kidney failure and so forth.

And we can look at the phase 3 trials to see if they are -- there has been a requirement in the regulations since, I think, 1994 that sponsors submit a gender analysis with their application.

Ms. Schakowsky. Is this incorrect, then? It says women comprise only 24 percent of participants in all heart-related studies.

Dr. Woodcock. Well, that may be true. And that may also include medical devices. It also may have to do with this age disparity when onset of disease.

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Ms. Schakowsky. I really hope that you will look at that because it is a great concern. It is a growing problem for women.

And let me just give you an example of what -- she said women, because we have different symptoms of heart disease -- she said, if you have some of these symptoms of nausea, dizziness, go to the emergency room, but say, "I am having chest pains" because, without that, you may not get an electrocardiogram and you may be misdiagnosed. We need to help women.

Thank you. I yield back.

Mr. Pitts. Chair thanks the gentlelady.

Now recognize the gentleman from Louisiana, Dr. Cassidy, 5 minutes for questions.

Dr. Cassidy. Hello, Dr. Woodcock. I always enjoy your testimony.

Dr. Woodcock. Thank you.

Dr. Cassidy. I mean that as a big compliment.

So, next, real quickly -- because I want to talk about something else -- but does FDA -- you mentioned that some institutions may be nervous about their liability if they refer their IRB activity to a centralized IRB.

Dr. Woodcock. Correct.

Dr. Cassidy. Except so many do, we know that is a false argument. Is there any way FDA can reassure those institutions? Because

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the gentleman from Mayo suggested it is a cultural issue. He didn't mention anything about legal. Thoughts?

Dr. Woodcock. Right. Yes. I heard his testimony.

I think that -- in my experience, that there are legal -- there are concerns of the -- counsel of the various --

Dr. Cassidy. Attorneys are always nervous. Right? I mean, they don't make money if they are not nervous. I hate to be cynical, but --

Dr. Woodcock. Yes.

Dr. Cassidy. Is there any way you can send -- FDA can send reassurances regarding that?

Dr. Woodcock. Well, we have tried. In guidance and so forth, we have encouraged this. And in the city initiative, we had a whole discussion and dissemination of information about central IRBs. But possibly there is more that we can do to encourage this.

Dr. Cassidy. Okay. Let me then bring on -- go back to -- you mentioned something intriguing earlier, that there may be some at high risk for disease; so, therefore, they will be more risk-tolerant.

Dr. Woodcock. Yes.

Dr. Cassidy. Now, I have a family member, a nephew, with Down syndrome. And I am looking on the alzheimers.org Web site, and they mention how virtually 100 percent of adults with Down syndrome by age 40 will have evidence of the tangles associated with Alzheimer's.

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Dr. Woodcock. Uh-huh.

Dr. Cassidy. Now, what are the issues regarding -- wow. This is a group of adults who are at risk -- 100 percent at risk for a terrible condition.

Dr. Woodcock. Right.

Dr. Cassidy. But there are other issues involved as well.

What are your thoughts about this? How do we make stuff available for folks incredibly at risk for such a terrible disease?

Dr. Woodcock. Yes. Well, with Alzheimer's, there are a number of problems. The basic problem is we still don't understand the disease well enough and the interventions that have been tried, which have been in late-stage disease when people are already demented, have failed to work.

Dr. Cassidy. Now, as I gather, though, the problem is predicting at an earlier stage those at risk. Correct?

Dr. Woodcock. That is correct. If you want to intervene early. We recently issued a draft guidance saying that, okay, if you want to intervene earlier, we would accept an end point that is subtle cognitive testing.

Dr. Cassidy. I accept that.

But how do you decide which population is at such high risk? Because, if you have a control group -- you follow what I am saying? -- only 10 percent are really going to be at risk.

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Dr. Woodcock. Right.

Dr. Cassidy. You with me? This is a really expensive study.

Dr. Woodcock. That is right. And so we advocate techniques called enrichment, which you try to use biomarkers or other tests to figure out. There are genetic conditions that increase your risk for Alzheimer's disease.

Dr. Cassidy. So speaking of Down syndrome as one example?

Dr. Woodcock. That would be one example. Yeah. There are others.

Dr. Cassidy. And can you give us the progress of that. So if you accept these, are people now using these?

Dr. Woodcock. Well, we need agents to use them in. So that is part --

Dr. Cassidy. And I am sorry. "Agents," you mean as in --

Dr. Woodcock. I am sorry. Investigational interventions that we can test in the people.

And that is part of the problem. The science of understanding what causes Alzheimer's and what you can intervene in that would actually delay or, you know, prevent the disease is not mature enough.

And we don't have really -- we have approved a couple imaging agents for Alzheimer's, but they aren't 100 percent. And you would maybe be kind of advanced --

Dr. Cassidy. But, for example, I know hyperinsulinemia is

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thought to be a potential risk factor.

Dr. Woodcock. Uh-huh. I know that.

Dr. Cassidy. And I think there are some studies suggesting that Actos might give some benefit.

Dr. Woodcock. Uh-huh.

Dr. Cassidy. Presumably, it would be at an earlier stage, not a later stage, would be a non-metabolic syndrome indication for the use of Actos. Fair statement?

Dr. Woodcock. Uh-huh.

Dr. Cassidy. Now -- so there is at least some of that. I guess I pose that to ask the degree to which that has been, again, the current state. I will go back to what is the current state of using that sort of thing?

Dr. Woodcock. Right. So the current state, we would -- if someone decided to do a trial -- and I believe there have been some intervention trials, not of Actos, but an earlier intervention at high-risk -- in higher-risk people -- they might identify people they felt were high risk for one reason or another, randomize them to this intervention or not, and then we would allow use of neurocognitive testing even before they had symptoms, if they had subtle changes, and if the treatment group did better than the placebo group, we could give accelerated approval.

Dr. Cassidy. So you are -- I guess you have got the framework.

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It is just a question of someone coming forward to take advantage of it.

But how long would such a study, do you imagine, take to complete its course? 20 years?

Dr. Woodcock. No. No. But we need to have better measurements that stick to these biomarkers and other measurements, like of subtle cognitive function, where we -- you know, the NIH and us and others are working on this.

Because the earlier you can intervene -- if you have a very targeted test that can identify people early, they don't have any symptoms, but you can tell their brain isn't working as well as it should, and then it will decrease over time. So that is kind of the rate-limiting step.

But I agree. Prevention is very difficult because there you want to intervene on people who are well and treat them for a long time and expose them to something with the hope that, at the end of the day, they are not going to get whatever bad outcome.

Dr. Cassidy. We are out of time. Thank you very much.

Mr. Pitts. Chair thanks the gentleman.

Now recognize the gentleman from Virginia, Mr. Griffith, 5 minutes for questioning.

Mr. Griffith. Thank you very much, Mr. Chairman.

Dr. Woodcock, as others have said today and, also, what I have

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heard in some of our informal conversations is that you not only do a good job as a witness, but that you are doing a good job overall.

Dr. Woodcock. Thank you.

Mr. Griffith. And so I appreciate that, and thank you so much for being here today.

I will tell you -- you and Dr. Cassidy had a little conversation about lawyers. Some lawyers are always nervous. Other lawyers are always looking for a way to find a way to solve the problem.

And so maybe we need to get some of those lawyers on your team and some of the corporate teams to solve the problem, figure out how we can make these things work, because I do think it is important.

As you probably know, I am one of those who advocates that we try to move a little quicker in those areas where we have problems that we don't have solutions for currently and, also, favor what is known in some State laws as right to try when you have a situation where doctors have tried everything and folks are given a diagnosis they have got, you know, months to live or their condition is going to be fatal.

I am one of those people who believes that we ought to let them go ahead and try whatever it is they are willing to pay to do because the FDA can't protect you if you are going to die from something that might kill you.

Dr. Woodcock. Right.

Mr. Griffith. I mean, it is going to happen one way or the other.

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You might as well have the right to try something.

That being said, I know there are a lot of issues surrounding that. I am not sure we have time for that today -- for that discussion today.

And I know that there is another panel, and I want to hear from the patients as well because they are involved in this process.

So respecting you greatly, I yield back my time.

Mr. Pitts. Chair thanks the gentleman.

Now recognizes gentlelady from North Carolina, Mrs. Ellmers, 5 minutes for questions.

Mrs. Ellmers. Thank you, Mr. Chairman.

And thank you, Dr. Woodcock, for being with us again today.

You know, this is such an important issue. As you know, we had our panel on Wednesday. And it seemed to me that it was a general consensus that everyone is looking for ways, you know, to expedite this and to make it more efficient and get those drugs to market sooner so that we can be taking care of our patients more effectively.

In your testimony and in the discussions that we have had today, you have touched on the biomarkers and targeted drug development to benefit disease populations, obviously.

You know, as all of our representatives here, we all have constituents with rare diseases, heart-breaking. Especially right now in my community, I have a very good friend with ALS. And as I am learning more and realizing, we have had a number of our -- members

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of our community diagnosed with ALS. So this is something that is very important to me right now.

And I am just looking at the idea -- as far as the target approval process being appropriated and applied through the FDA, it seems to be that we are looking at cancer and HIV. Where do some of those rare diseases fall within that?

And, you know, you had mentioned and there was discussion about the master protocol and that seems to be applied more to cancer or HIV. Where can some of the rare diseases fall in there? And what can we do to help make that happen?

Dr. Woodcock. Well, any rare disease would be a great candidate for a standing network, a network of experts -- and I think you may hear more about this from the next panel -- where they are ready to evaluate any therapy that advances through the early, the nonhuman, stages.

So they could pick that up right away and test it quickly. And that -- in the meantime, until that happens, they can get what we call natural history, which I know sounds very wonky.

But, you know, people are asking -- just now Mr. Cassidy -- like how long does Alzheimer's progress from presymptomatic to symptomatic. Well, we need to know that so that we can design the trial correctly.

In rare diseases, even more difficult because nobody knows. And, usually, they get experts together and say, "Well, in my opinion, it

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takes this long." Right? And they are usually wrong because they have only seen a few people.

So we are encouraging these natural history studies, these networks. First, they look at the people and they can look at the biomarkers, too.

So what changes in ALS? What can we measure? Could we measure something that gives us indication that treatment might be working? Right?

And then, as soon as a therapy becomes available, then you can rapidly get people into a trial and there would be no delays because there is no delaying an ALS.

Mrs. Ellmers. Right. Exactly.

And that is, you know, obviously part of the concern. And certainly I agree with my colleague in talking about right to try. You know, this would be a perfect example of decisions that families and patients can make.

I do want to talk about -- you know, you had also mentioned listening carefully to patients and families.

Dr. Woodcock. Yes.

Mrs. Ellmers. And, you know, do you consider and give more weight -- I mean, that is one of our questions, is, you know, how much weight are you giving to the patients and families? And what -- there again, from our perspective in Congress, what can we do?

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You know, as we have heard everyone agreeing that we need to make a difference here and we can move things forward, how open is the FDA to this possibility? And what can we do right now to make this happen?

Dr. Woodcock. Well, as I said in my testimony in the beginning, you know, medical culture has changed over the years. It used to be very doctor-centric -- okay? -- and now it is patient-centric. And the FDA culture and drugs is a medical culture. And so that has changed at the same time, but slowly.

So we have been working, though, very diligently with patient groups and so forth to try to get the patient point of view more central to the evaluation of benefit and risk and what it means to the person who actually has the disease, is going to take the drug.

To answer your question what can be done, I think a lot of this needs to be done out in the community. The patient groups need to get organized and develop these. Some of them are working with PCORI and trying to use that mechanism to get more information available and so forth.

We have gotten draft guidances from different groups, including Muscular Dystrophy, that really are a statement of, "This is what we care about. This is what we value. This is what we want you to look at." And we will pay extremely close attention to those, and those are extremely valuable.

Mrs. Ellmers. Thank you, Dr. Woodcock.

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And I yield back the remainder of my time.

Mr. Pitts. Chair thanks the gentlelady.

We are voting on the Floor. We have 10 minutes left in the vote.

We have three more questioners.

Mr. Guthrie recognized for 5 minutes for questioning.

Mr. Guthrie. Thank you, Mr. Chairman. I will try to be brief.

I will echo what the others said about your testimony.

Appreciate it.

But since we started this 21st Century Cures and -- everybody's excited. Both sides are trying to see how we can do this better.

And I have heard from a lot of groups and I have heard from -- several times that the oncology division seems to be one people really like to work with and it works well. Some of the other divisions in expedition is not as well to work with.

And I have always believed -- Jack Kemp used to say, "Don't study failures and point out the problems. Let's look at successes and see how it can be replicated."

So within your own agency, you are having wonderfully successful programs, at least according to the feedback I have gotten, and some not as fun, I mean, as the ability to work with.

So I guess my question is: Is there any impediment to saying, "Hey, this" -- the oncology is what we hear about more, not that the others aren't, but we hear more -- is there any impediment to taking

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what is happening there and transferring to other agencies? Is there something Congress can do to make it easier or is it just learning and moving forward?

Dr. Woodcock. You know, let me tell you that 10 years ago, you know, I heard a lot of negative comments about oncology -- our oncology group. All right? And now we have therapies that are so effective. They are just -- they are really on fire.

They see that, for their patients they took care of -- they are all oncologists, hem onc doctors -- that these new treatments would really have made a difference for those people. And so they are doing everything they can to get those treatments out.

And I think what we need, we need the same kind of inspiring therapies in these other areas. And I do think the doctors -- they are doctors. They are physicians. They care about patients in their disease area.

And this -- this breakthrough -- I don't know whether you can see it here, but you see that other disease areas are coming up and we are designating -- in neurology and anti-infectives and psychiatry, we are designating potential breakthroughs. And so this type of thing will really help.

But, also, of course, we try to have a management structure, multiple mechanisms whereby we have consistency and uniformity of our approach and our procedures, and I think we do quite well in our

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procedures.

But I think underlying -- sort of the attitude may have something to do with the underlying science. We had a war on cancer. It is starting to pay off. And we need to really expedite that.

Mr. Guthrie. Well, thanks.

And I have a bill particularly to put the same status for -- professional budget judgment status for Alzheimer's, which would -- we are going to spend in 2050 \$1 trillion. This is not loss of income, loss of productivity.

Dr. Woodcock. Right.

Mr. Guthrie. That is \$1 trillion spent on that disease.

That is when I am 86. So that is when my children and our grandchildren will be taking care of us. So, hopefully, we can have the same inspiration and do that, particularly in Alzheimer's.

Dr. Woodcock. I can assure you that, if they were promising treatments for Alzheimer's, we would jump right on them.

Mr. Guthrie. Appreciate that. Thank you very much.

And I will yield back.

Mr. Pitts. Chair thanks the gentleman.

Recognizes the gentlelady from Tennessee, Mrs. Blackburn, 5 minutes for questions.

Mrs. Blackburn. Thank you so much, Dr. Woodcock. I have basically one question that I do want to get to.

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Looking at the QIDP and the moving forward of that, it can give up to 5 years of additional data exclusivity. Bipartisan effort. We were all for it.

What I want to know from you is: How many QIDPs has the FDA designated to date? How many products have actually been approved to date? And do you believe that the QIDP is an important designation?

Dr. Woodcock. It is absolutely important.

Mrs. Blackburn. Okay.

Dr. Woodcock. We have granted 50 designations for 34 unique molecules. And in the last several weeks, we have approved the first two medications that are designated, the first two antimicrobials.

Mrs. Blackburn. Excellent.

Dr. Woodcock. So that is making a difference. We do feel, though, that probably more needs to be done.

Mrs. Blackburn. And in that "more needs to be done," give me a couple of examples of what you think the next step should be. I would be interested in that.

Dr. Woodcock. Well, we are very interested in the pathway that people call limited population antibacterial drugs or other streamlined pathways for development that would be matched with some sort of symbol or logo that would enable doctors and other prescribers to recognize that it was from a limited program. We think that would also allow us to streamline the development program.

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Mrs. Blackburn. Excellent.

And I just, for the second panel, want to welcome a fellow Tennessean, Dr. Marshall Summar, who is going to be speaking on behalf of the National Organization of Rare Diseases.

So welcome. We are delighted you are here.

And I would yield back.

Mr. Pitts. Chair thanks the gentlelady.

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

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

And thank you for your testimony, Dr. Woodcock.

I asked these questions a few months ago and I didn't get a response. So I am going to see if I can get a response this time. Appreciate it if you can answer.

Can you tell me how many treatments were approved with novel biomarkers used for the first time?

Dr. Woodcock. No. I don't have that in the --

Mr. Bilirakis. Can you get that information to me as soon as possible?

Dr. Woodcock. I would be happy to. It is a very interesting question. Yes.

Mr. Bilirakis. And then next question: Have any accelerated approval occurred within novel biomarker in never-before-treated

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disease?

Dr. Woodcock. Oh, yes. All the time. And I can get that for you. I don't have it, again.

Mr. Bilirakis. Please.

How many new biomarkers did the FDA accept for a first-time use in the last 5 years?

Dr. Woodcock. Certainly.

Mr. Bilirakis. Can you get that for me?

Dr. Woodcock. Absolutely.

Mr. Bilirakis. Okay. Very good. Thank you very much.

I know we don't have a lot of time; so, I will yield back. Thank you, Mr. Chairman.

Mr. Pitts. Thank you.

There is 2 minutes left in the vote on the Floor; so, we are going to recess. There are two votes. As soon as we have the second vote, we will come back and reconvene with our second panel.

Again, Dr. Woodcock, thank you for coming. You have been a terrific witness.

Dr. Woodcock. Thank you.

Mr. Pitts. Members will have follow-up questions. We will send them to you. We would ask that you please respond.

[The information follows:]

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Mr. Pitts. Thank you. And thank you for your patience.

The subcommittee stands in recess.

[Recess]

Mr. Pitts. Time of recess having expired, we will reconvene the subcommittee on Health and introduce our second panel.

In our second panel, we have five witnesses. I will introduce them in order of their presentation. First, Ms. Pat Furlong, Founding President and CEO of the Parent Project Muscular Dystrophy; second one, Mr. Robert Beall, President and CEO of Cystic Fibrosis Foundation; third, Mr. Richard Pops, Chairman and CEO of Alkermes; fourthly, Dr. Leonard Lichtenfeld, Deputy Chief Medical Officer of American Cancer Society; finally, Dr. Marshall Summar, Director of Scientific Advisory Committee, National Organization for Rare Disorders.

Thank you all for coming. You will each be given 5 minutes to summarize your testimony. Your written testimony will be placed in the record.

Ms. Furlong, we will start with you. You are recognized for 5 minutes for your opening statement.

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STATEMENTS OF PAT FURLONG, FOUNDING PRESIDENT AND CEO, PARENT PROJECT MUSCULAR DYSTROPHY; RICHARD F. POPE, CHAIRMAN AND CEO, ALKERMES; MARSHALL SUMMAR, M.D., DIRECTOR, SCIENTIFIC ADVISORY COMMITTEE, NATIONAL ORGANIZATION FOR RARE DISORDERS; ROBERT J. BEALL, PH.D., PRESIDENT AND CEO, CYSTIC FIBROSIS FOUNDATION; J. LEONARD LICHTENFELD, M.D., DEPUTY CHIEF MEDICAL OFFICER, AMERICAN CANCER SOCIETY

STATEMENT OF PAT FURLONG

Ms. Furlong. Thank you.

Good morning, Chairman Pitts and members of the committee.

My name is Pat Furlong. 20 years ago I joined other parents to form Parent Project Muscular Dystrophy to end Duchenne, one of the many forms of muscular dystrophy and the most common lethal genetic disorder diagnosed in childhood.

In 1984, I received the horrific diagnosis on my two sons, Christopher and Patrick, and both of my sons are gone now. I wage this crusade in their honor.

Much has happened over the past 15 years to transform the Duchenne clinical and research landscapes, and much of this is a direct result of the actions by Congress and this committee, notably the enactment of the Childs' Health Act in 2000, and the Muscular Dystrophy CARE Act

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1 year later. Since the MD CARE Act was enacted, we have seen about 10 years added to the lifespan of patients with Duchenne.

There has been an improvement in quality of life driven largely by the development and dissemination of care standards so that all patients can be diagnosed accurately and as early as possible and provided with the highest quality of care.

The MB CARE Act also transformed the Duchenne research landscape. What was just 12 years ago a near-barren field has evolved into a robust area of research where multiple potential therapies are in clinical testing and several others are in early stages of development.

Despite these advancements, Duchenne remains a fatal disease without any FDA-approved therapies. Most boys end up in wheelchairs by their mid-teens, and only a few live beyond their late 20s.

Our community needs therapies and we need them fast to. To achieve this goal, PPMD has led groundbreaking efforts over the past year to address two major impediments in our request to end Duchenne.

One is a lack of regulatory understanding of patient and parent perspectives on benefit-risk; and, two, a lack of clear guidance or direction to the biopharmaceutical companies designing these clinical trials.

PPMD partnered with Johns Hopkins University to conduct the first-ever scientific survey on benefit-risk perspectives. The survey involved 120 parents of Duchenne children. It validated what

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we have known anecdotally for years.

Because Duchenne is 100 percent fatal at a young age, many patients and families are willing to accept higher levels of risk in return for the prospect of potential benefit.

The data has been shared with the FDA and was recently published in an academic journal. Now the FDA must ensure its reviewers apply this evidence to their decisionmaking process.

Another impediment to drug development, particularly in rare diseases, is the absence of a clear guidance from FDA when it comes to designing clinical trials. Small patient populations, limited knowledge about the condition and a lack of accepted or validated biomarkers are some of these challenges.

At the invitation of the FDA, PPMD led a comprehensive 6-month effort to convene key stakeholders -- patients, parents, clinicians, researchers and industry -- to write a draft guidance document that would address trial design and many other issues. This was submitted to the FDA last month, marking the first time a patient group has led the development of such a product.

Now the FDA must step up promptly to review the draft, gather stakeholder input and issue a guidance document under the Agency's name.

While each of these projects is focused on Duchenne, each also offers a template or a model that could be applied to other diseases

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or other conditions, particularly rare diseases, and I hope other organizations will take on similar programs.

So what can Congress and Federal agencies do moving ahead? First, you can make sure that the patient perspective on benefit-risk and other issues is considered by reviewers of the FDA.

One way to do so could be by establishing a nonburdensome step where reviewers would disclose how they did or did not take such information into account making their decisions on a drug application. This would shed light on for what many considered a mysterious process and could be done in a very simple manner.

Second, I suggest an even greater focus on regulatory science so the FDA keeps pace with the breakneck speed of innovation. Specifically, NIH could bolster support for regulatory science research and infuse that into clinical and translational awards. Incorporating a regulatory perspective earlier in the pipeline can maximize the likelihood that candidate therapies will be ready for the rigor of the FDA.

Finally, I would encourage greater flexibility in clinical trials, particularly rare fatal conditions like Duchenne that have small populations. Business-as-usual trial designs simply do not hit the mark when working with these populations.

The Duchenne community has traveled a great distance over the past 15 years, thanks in significant part to the leadership of this very

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committee, leadership that will continue on Monday with action by the full committee on the MD CARE Act amendments.

For far too many families, my own included, this journey has not been fast enough. We stand ready to work with your committee to make sure the 21st Century Cures Initiative ends Duchenne and so many other rare diseases.

Thank you.

Mr. Pitts. Chair thanks the gentlelady.

[The statement of Ms. Furlong follows:]

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Mr. Pitts. Mr. Beall, you are recognized for 5 minutes for your opening statement.

STATEMENT OF ROBERT J. BEALL, PH.D.

Mr. Beall. Thank you very much for this invitation to present this testimony.

The story of cystic fibrosis is clearly a story of determination of hope and optimism. The progress that we have documented in our submission really shows what is possible when a system works well, when patients, when stakeholders and the regulatory agencies collaborate to develop life-changing treatments.

Cystic fibrosis is clearly a life-threatening genetic disease that affects about 30,000 individuals in the United States. There has been tremendous progress in life expectancy over the decades.

In the 1950s, people with cystic fibrosis barely lived to elementary school. But there are people that are living today with cystic fibrosis in their 30s and 40s, and some are even going beyond.

But we still lose too many patients at very young ages. The increase in life expectancy is due in large part to groundbreaking advancements and treatments made possible because of the Cystic Fibrosis Foundation, our patient community and our industry collaborators.

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2 years ago the FDA approved Kalydeco, the first drug to treat the underlying causes of cystic fibrosis in a small subset of people with the disease. Hailed as a game-changer, it has transformed the lives of those taking this drug.

It is a perfect example of personalized medicine. I might mention that the FDA approved this drug in near record time, 3 months before the prescribed PDUFA date and months before the EMEA.

Just 2 weeks ago we saw another breakthrough in cystic fibrosis. It happened when -- the positive data from a phase 3 clinical trial for a new therapy that is targeted at 40 percent of the CF population.

This data was released by Vertex Pharmaceuticals Company. You know, these products would not have been possible without the breakthroughs that have taken place in basic research, in all the efforts that our foundation has made over the years.

The CF community was thrilled to learn that the trial participants showed a significant improvement in lung function, weight gain, and 30 to 40 percent reduction in exacerbations. That is the time that they would have to go to the hospitals or have IV infections.

So this is clearly a game-changer for these patients. Obviously, Vertex plans to submit the new drug application to the FDA by the end of the year for this treatment.

What is exciting about this progress is that these drugs would not have been possible were it not for the Foundation and our patient

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community. Our commitment to scientific discovery and drug development is at the root of our success, but it hasn't been easy and it hasn't occurred overnight.

In 1965, we created the first patient registry in the United States, now a model for chronic disease. Because of this registry, we have a documented natural history of cystic fibrosis.

We have the mutation analysis on most of these patients, as Dr. Woodcock referred to this morning, and we have the ability to have post-marketing phase 4 follow-up on these new drugs as they are introduced to the community.

The same year, 1965, we created a care center network. 90 percent of all patients seen in the United States are seen at these CFF-accredited and funded care centers.

In 1989, through our support, the CF gene was discovered, 12 years before the human genome was completed.

In 1998, we established a Clinical Trials Network, the first Clinical Trials Network founded solely by a nonprofit organization like the Foundation. It is a critical component of our ability to conduct CF clinical trials efficiently and effectively.

In 1999, the CF Foundation pioneered a successful venture philanthropy model to derisk companies from investing in CF research drug development.

It was our initial investment of \$42 million in a small biotech

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company in San Diego that ultimately led to Kalydeco. Vertex would not have had Kalydeco and the other drugs announced last week were it not for the Cystic Fibrosis Foundation.

The CF Foundation spearheads collaboration across all sectors, and this same collaborative spirit extends to the Foundation's strong partnership with the Food and Drug Administration.

With the FDA, we are committed to collaboration and bringing strong data to the table. As often has been stated, the CF Foundation comes with data, not demands.

Just last week we met with FDA officials to discuss strategies for clinical research design that may not occur until 5 years from now.

However, curing a disease is never easy, and even more risky is the approval of drugs without sufficient data to assure efficacy and safety.

If this happens, you place patients immediately at risk and you risk losing the opportunity to test drugs that could have a real impact and beneficial effect.

So, in closing, what can Congress do for us? Congress should make sure that patients have a seat at the table, as was just referred to.

Congress must provide the necessary resources so that the FDA can attract the best and the brightest. And Congress must provide the NIH and FDA sufficient resources for regulatory sciences, as also mentioned.

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But, finally, Congress may also encourage that they look at the CTSA program, a network of care centers that are funded by the NIH, and see how they might use these to be able to facilitate Clinical Trial Network and the development of patient registries in other rare diseases.

So, once again, thank you for this opportunity to add the CF community's perspective to this important discussion.

Mr. Pitts. Chair thanks the gentleman.

[The statement of Mr. Beall follows:]

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Mr. Pitts. Mr. Pops is recognized 5 minutes for an opening statement.

STATEMENT OF RICHARD F. POPS

Mr. Pops. Thank you very much.

I would like to thank you, Mr. Chairman, Ranking Member Pallone and all the members of the committee for inviting me to testify.

I just want to thank Chairman Upton and Congressman DeGette for spearheading the 21st Century Cures Initiative.

I would also like to express my respect for and appreciation for the folks on this panel and for Dr. Woodcock. We are all partners in this together, and it is an credibly important mission.

The simple and powerful concept of incorporating insights from patients is centrally important to the future of the Nation's healthcare system. And it is also one of the great opportunities for us all to have a transformative impact.

I have served as the CEO of Alkermes for over 20 years. Our company develops medicines for people living with chronic debilitating diseases, such as opioid addiction, schizophrenia and depression. Our approach is entirely dependent upon considering the patient perspective early and consistently throughout the drug development process.

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I also serve on the Boards of both BIO and PhRMA and was deeply involved in the PDUFA V negotiations, as well as the preparations ongoing for PDUFA VI, where elevating the patient voice has already emerged as a key theme for that initiative.

Today I would like to propose a new framework for patient involvement in developing new medicines, which requires engagement from all three of the major parties involved, innovative biopharmaceutical companies like ours, FDA and the patients who stand to benefit from these medicines.

And the framework is based on three core principles.

First is that interactions must be data-driven, based on science other than the -- and separate from powerful and passionate advocacy messages that patient groups otherwise deliver.

Second, the engagement framework should be actionable, not theoretical. It should improve the overall efficiency of the process rather than adding new steps in a process that is already incredibly complicated. This is particularly important for young biotechnology companies who are developing their first drugs on limited resources.

Third, the approach should preserve and enhance FDA's gold standard of safety and efficacy, which is really one of our great national treasures. I believe deeply, personally, that increased patient input can coexist with efficiency and the highest level of scientific rigor.

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So from industry's perspective, there is clearly no consistent way to incorporate patient-generated input. This input would have a really meaningful impact on a range of critical decisions we and our researchers make specific to particular product candidates and certainly to the way we design clinical trials and implement them around the world. This is an important missing link.

As Dr. Woodcock mentioned and the FDA, patient engagement is not a new concept. Several provisions included in PDUFA as well as FDASIA have resulted in meaningful new expansions in patient engagement.

FDA has also been open to and has taken initial steps to include patient input into their reviews, and we can build on this. The proposed framework I am considering would build on all of these things.

The historical paradigm of drug regulation as a bilateral process between FDA and the industry is outdated. Science and society have continued to advance. Patients are organizing in new ways, and their critical role in driving innovation is becoming more the rule than the exception. We have 20th-century regulatory framework for 21st-century drug development.

To tackle these increasingly complex scientific and regulatory issues as we look to treat and cure complex diseases, all three parties can work together to develop improvements to their existing regulatory framework.

These would include new clinical trial designs, more efficient

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clinical trial enrollment methods, advancing FDA's evaluation of risk and benefit, and more sophisticated post-market data collection. These are incredibly exciting areas for future consideration.

We would need to evolve the way we work together, all the different parties, recognizing our shared responsibility to improve the efficiency of the development process and our accountability to assure the medicines are safe and efficacious for patients.

There will be a number of challenges to this as we move in, and these could include establishing a common threshold for data and scientific rigor that is shared by patient industry groups and FDA, modifying existing regulations to accommodate this new framework, protecting intellectual property and data, which is essential to enabling innovation and maintaining this gold standard of safety and efficacy.

As next steps, I propose that Congress, industry, FDA and patient groups come together to develop and implement this new framework, building on existing patient-focused provisions of PDUFA and FDASIA. We should also analyze existing statutes and regulations to identify impediments and opportunities.

In conclusion, the concept of a new and comprehensive patient-inclusive framework is both ambitious and, at the same time, it is quite modest.

It is ambitious as it could result in a dramatic change in the

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way we discover and develop medicines. It is modest because it is not a new regulatory pathway or authority, but it builds on an existing foundation.

And we at Alkermes and all of our colleagues in the biopharmaceutical industry are standing by to help you in that effort. We really thank you very much for your leadership.

Mr. Pitts. Chair thanks the gentleman.

[The statement of Mr. Pops follows:]

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Mr. Pitts. Dr. Lichtenfeld, you are recognized for 5 minutes for your opening statement.

STATEMENT OF J. LEONARD LICHTENFELD, M.D.

Dr, Lichtenfeld. Good morning, Chairman Pitts, Ranking Member Pallone and members of the subcommittee.

I am Dr. Len Lichtenfeld, and I am Deputy Chief Medical Officer for the American Cancer Society and truly appreciate the opportunity to be with you today to testify. The American Cancer Society is pleased to contribute to the dialogue around the committee's 21st Century Cures Initiative.

Today I would like to focus on three critical areas for the committee's consideration. One is the need for greater investment in research; secondly, expedited approval processes that continue to ensure safety and efficacy of approved drugs; and, third, making patients active partners in all aspects of research development and regulation of new therapies.

We are fortunate and blessed that today we have 14 million cancer survivors in the United States. It is a remarkable number, and it is due to more effective treatments and improved screening tools that have been made possible through research.

We must continue and expand our steadfast commitment to research,

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and we must continue to support researchers working on finding the next generation of cures.

Just as important, we must ensure that expedited approval processes for drugs and devices are appropriately safe, effective and accessible to patients. The goal of the 21st Century Cures Initiative is to accelerate the development and approval of new medical treatments.

There are a few other areas that can match the research and development activity in the field of cancer. It is, in fact, and has been a model of innovation.

The FDA's Office of Hematology Oncology Products has aggressively used the tools provided by Congress to speed new drugs to patients and has encouraged drug companies to be innovative in clinical trials.

In the past 8 months, three cancer drugs have been approved using the accelerated pathway. One approval was based on a trial of 111 patients, an example of research approvals happening faster and with smaller clinical trials as has been the case in the past.

Small-sized trials and accelerated approval do have drawbacks. They may not include a diverse population, which may yield an incomplete picture of how a drug might work in a broader population. Small trials and accelerated approvals also tend to be seen in deadlier cancers where there are no other good therapeutic options.

And I want to stress that the risk-benefit tolerance of a cancer

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patient facing a poor prognosis may be much different than for those with other available treatment options.

And, therefore, the same acceptance of reduced data on which to base FDA approval may not be appropriate in other fields or for other diseases.

Finally, I want to stress the importance of researchers, pharmaceutical companies and the FDA in engaging widely and meaningfully with patients.

The Food and Drug Administration Safety and Innovation Act requires greater patient involvement throughout the drug and device approval process. ACS CAN championed provisions to expand the FDA's patient representative program to maximize patient input during the drug development process.

We need to continue to build on that progress. Patients can provide important perspectives at various stages of medical product development and regulation.

They know more than anyone what is most important to patients, to themselves: Symptom reduction, risk tolerance and design elements that might affect trial recruitment or retention.

This kind of patient involvement should be reinforced and supported and, to this end, the FDASIA provisions requiring FDA to address challenges that have hindered patient involvement must be fully implemented.

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We urge the committee to consider examining opportunities for providing greater funding to support the FDA patient representative program as well as broader continued engagement with the patient community.

Another important way patients' perspectives can inform development of therapies is through the design and use of patient-reported outcomes.

Measures of cancer therapy effectiveness sometimes include functional status, pain or quality-of-life measures, but these may be reported by the physician rather than by the patient.

Quality-of-life measures like pain or nausea should come from patients themselves, and patients should help prioritize the importance of these side effects in the overall response to a disease and the associated treatments.

When quality-of-life outcomes are vigorously measured and supported by the FDA, they should be included in a drug's labeling and they should be considered for a drug's approval.

The FDA should also be encouraged to work with industry and researchers to incorporate self-reported symptom measurements as a regular part of clinical trials.

In closing, we appreciate the opportunity to contribute to the dialogue around the committee's 21st Century Cures Initiative and look forward to working with the subcommittee and its staff. I am happy

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to take any questions.

Thank you very much for this opportunity.

Mr. Pitts. Chair thanks the gentleman.

[The statement of Dr. Lichtenfeld follows:]

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Mr. Pitts. Dr. Summar, you are recognized for 5 minutes for your opening statement.

STATEMENT OF MARSHALL SUMMAR, M.D.

Dr. Summar. Thank you, sir.

Good morning, Chairman Pitts, Ranking Member Pallone and members of the subcommittee. And thank you for inviting me today.

My name is Marshall Summar. I have the good fortune to be the Chief of Genetics and Metabolism at Children's National Medical Center here in Washington, D.C.

I have been working in the field of rare diseases for the last 29 years, and I am here today in my capacity as a member of the Board of Directors of the National Organization of Rare Disease and Chair of the Scientific Advisory Committee of NORD.

On behalf of the estimated 30 million individuals with rare diseases, NORD thanks you in the Energy and Commerce Committee for your continued strong support of the rare disease community. You have made a huge difference for us.

NORD's a unique federation of over 200 patient advocacy groups, clinicians, researchers, dedicated to helping people with rare diseases.

NORD provides resources, research advocacy, education, community

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and infrastructure support to the rare-disease community that small individual organizations cannot. It is the nature of rare diseases. They are small.

NORD was founded in 1983 and played an active role in the passage of the Orphan Drug Act, which is a successful model of how to incentivize the development of treatment that saves lives.

Data show that years of life lost to rare diseases declined at an annual rate of 3.3 percent after the Orphan Drug Act due to the development of new treatments.

Without these new drugs, if you take them out of the equation, the number of years of lives lost should have increased at about a 1 percent rate per year. So it has made a real impact on our patients.

Speaking personally, without these treatments, many of my patients would not be here. I thank you for what you have already done.

These efforts represent a good beginning, but there is much more we can do to improve the lives of our patients, and NORD views the 21st Century Cures Initiative as a great way to do this.

NORD's long advocated increased involvement of patients in the drug development process. We appreciate the commitment by many at the FDA to increase patient involvement, but believe much more needs to be done to make patients feel they are partners in the process. NORD will continue to work with the FDA to advance the patient role in the development and approval process.

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We have developed a series of recommendations that we believe will advance not only the development of new orphan drugs and devices, but non-orphan ones as well. We look forward to discussing these ideas with the committee as the 21st Century Cures Initiative continues.

Permit me to focus on two of our recommendations.

First, we support the establishment of a commission and national plan to determine priorities, methods, resource needs and a consistent agenda on rare-disease registries and natural history studies.

They have got a lot of variation. They tend to be all over the map. To assess the drug's efficacy, we need the information on the existence, frequency and severity of clinical findings. This information is needed before a clinical trial can begin.

We encourage the creation and maintenance of programs to create, curate and standardize registries and natural history studies which can generate this needed data.

This could be one of the most important accelerators of the treatment development and monitoring process. These registries can also be used in the post-approval process as well.

This is an area where patients can have a major and cost-saving impact on the process. Patient-entered data has been shown to be accurate and useful when collected properly.

Creative hybrids using physician-, patient- and other health professional-collected data can greatly speed the understanding,

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discovery, approval and monitoring process.

In collaboration with the NIH and FDA, NORD has built and is in the process of testing a rare-disease patient-driven registry national history program. The NIH's Rare Disease Clinical Research Network has already demonstrated the benefits of this approach.

In a registry I have been involved with, we have had approval of three drugs over a 10-year period with only 700 patients. So it definitely has accelerated the approval process for us.

The Patient Centered Outcomes Research Institute is developing these statistical methods and models to use data from rare-disease patient studies that will further refine this process.

They are also involved in patient-driven registries through PCORnet and will begin working with NORD on our rare disease-focused registry program. So we should have good input from multiple agencies.

All of these efforts will help our patients, but a national plan and standards would help prevent duplicated effort and resources. This is what we truly need.

The other thing we advocate is significant reform to the Institutional Review Board system. I have been working with this system for the last 30 years; so, I am pretty familiar with all of its manifestations.

Currently, all clinical trials for new treatments, whether a drug, biologic or medical device, must receive approval from an IRB.

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Each institution and study site typically requires approval and protocol adjustment by its own IRB. With a large number of sites needed for rare-disease study, this is one of the greatest impediments and cost to clinical trials.

NORD recommends that Congress develop legislation that would derisk the process and foster the creation of an IRB system that is portable across institutions.

The de-risking of the IRB process and the encouragement requirement of reliance agreements between institutions receiving Federal funding would save cost and time while accelerating the clinical trials and clinical research process greatly. This will significantly increase the pool of study sites and allow greater patient participation.

These are just two of our recommendations. My written testimony includes the rest.

And I on behalf of NORD, I thank the committee for allowing us to testify today.

Mr. Pitts. Chair thanks the gentleman.

[The statement of Dr. Summar follows:]

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Mr. Pitts. Thanks to all the witnesses for your opening statements. And we will now begin questioning.

I will recognize myself 5 minutes for that purpose.

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RPTS MCCONNELL

DCMN WILTSIE

[11:32 a.m.]

Mr. Pitts. Ms. Furlong, we will start with you.

Do you believe your guidance collaboration with industry is a scaleable model that can be used in other conditions, specifically, where there are unique factors that make Duchenne muscular dystrophy guidance a special case in the multi-stakeholder effort that you led with encouragement from the FDA?

Ms. Furlong. Thank you, Chairman Pitts, for the question.

I certainly think that this methodology and process is exportable to other rare conditions. How we started the guidance or initiated the guidance was to develop a steering committee that was representative of the stakeholders, which included patients, academia, as well as industry.

From there, the steering committee identified several areas, seven working groups, actually, of things that they felt were relevant, to include diagnosis, biomarkers, clinical trial design, natural history, and benefit-risk.

And then we further developed a CAB, which is the Community Advisory Board, so that would be -- incorporate the entire patient voice and any individual or patient group that wanted to contribute

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to the development of the guidance.

The standardization for the guidance was that it would be a reference document and that it would include documented evidence that was published or accepted for publication by the end of July.

So we felt -- and we are writing up the methodology -- that this methodology is exportable. It was certainly an investigation and a thorough, thoughtful, reasoned look at the community and the nuances of Duchenne.

But I believe that most rare diseases could do the same. Their issues may be slightly different and their progress to date might be slightly different, but it is certainly exportable.

Mr. Pitts. Thank you.

Dr. Beall, communication with patients to make sure they can make informed decisions about clinical trial participation is critical.

How does the cystic fibrosis community communicate with patients about the various options? And how do you think we can best translate your good practices into the Cures Initiative?

Mr. Beall. Thank you very much.

First of all, we have -- because 90 percent of all of our CF patients are seen in a network of care centers and that we also have a Clinical Trials Network, there is a very close relationship between our physicians and the patients that are involved.

And that is critical for the recruitment of patients in the

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clinical trials. It is critically important for showing them the value and the risk of participating in clinical trials.

And it is that close association between the physician and the patient and the recruitment process in a very closed network that is critical. That is why I think Clinical Trials Networks are critically important.

So we also have established within our Clinical Trials Network a data safety monitoring board made up of -- it is independent of the Cystic Fibrosis Foundation, but it is made up of experts.

And that provides a degree of assurance to every single patient that there is somebody looking out for their continuing interest and for any risk that may be inherent in any single trial.

So I think all of these things, plus we have worked very hard to try to create a culture of participation and a responsibility that each patient, when you have a small patient population, needs to participate in the process. So I think it is that reassurance that is so important.

Mr. Pitts. Thank you.

Mr. Pops, what stage of drug development could most use the assistance of patient insight about benefit expectations and risk tolerance?

Mr. Pops. Thank you for the question.

It is actually the most exciting part of the whole opportunity, that it is every stage, actually from identification of new drug

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candidates, all the way through to determination of the value of the medicine after the completion of the pivotal clinical trials.

And I think that is the whole idea of this framework, is creating a structure where we can get that input on a continuous basis, and I think it could fundamentally transform the way we approach these development programs.

Mr. Pitts. Thank you.

Dr. Lichtenfeld, you have discussed examples of cancer drugs that have recently been successfully approved by FDA through an accelerated approval process.

Are there best practices that we can learn from cancer and how FDA is expediting the approval process for particular drugs?

Dr. Lichtenfeld. Thank you, Mr. Chairman.

When we talk about best practices, I think the question really came up with Dr. Woodcock earlier today: What is the oncology community doing that is different than other communities?

Let's understand it is a complex process in the sense that we have research that has been building literally for decades that has produced very exciting results that is actionable and companies are standing up to create drugs for the targets that we are finding for the new immunotherapies for genetic disease, what have you, genetic markers. So we are, in a sense, at an interesting and turning-point kind of place.

But important, relevant to your question, the Office of

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Hematology Oncology Products has also stepped up to the plate. And as was mentioned earlier, the oncology community appreciates the efforts of the FDA staff to reach out to the patient community, to reach out to the pharmaceutical community, to reach out to those who do clinical trials, to be active participants, to be at the table.

Lung-MAP was cited several times. The American Cancer Society was grateful to be able to have contributed to that effort, among many other organizations.

But the FDA has become an active partner with the process. And so I don't know if that is a best practice or a best example. But it is that source of communication.

But let's not forget it is also the opportunity because we are now in a place that we only dreamed of just a short while ago.

Mr. Pitts. The chair thanks the gentleman.

My time has expired.

The chair recognizes the ranking member, Mr. Pallone, 5 minutes for questions.

Mr. Pallone. Thank you, Mr. Chairman.

My questions are of Mr. Beall.

The Cystic Fibrosis Foundation has done some great collaborative work that has resulted not only in successful marketing of Kalydeco, but also the recent positive test results of a complementary drug that may extend treatment to nearly half of all patients with CF. And, of

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course, I commend you for your efforts.

But I wanted to ask you about a couple of points in your testimony. In your remarks, you spoke about the CF Foundation's strong relationship with the FDA and the importance of bringing good data to the table when consulting with the FDA, which I know is true. And I would like to hear more about that relationship.

Obviously, we are hearing a lot today about the need for FDA to do more to seek and incorporate patient input into its review process.

So the basic question, Mr. Beall, is: Can you tell us more about the CF Foundation's interaction with the FDA? And are there any lessons that can be learned by other disease groups?

Mr. Beall. Well, I can give you a perfect example because, on Wednesday of this week, we had three officials, including Dr. Robert Temple, who is in the drug division at our offices, talking about the development of clinical trial protocols of drugs that might not enter into clinical trials until 3 to 5 years from now.

So that is a perfect example of this open discussion. Because we have a natural history of the disease. We know that the drugs that we have tested are treating the basic defect. We know the mechanism of action. We have a safety profile.

And now we can start to talk about the future. And I think it is that kind of example. And that goes back many, many years.

Soon after we discovered the CF gene, we talked about gene therapy

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and we had extensive dialogues with the FDA, not only with manufacturers, but with the FDA and the Foundation.

So I could just say that we have always had a wonderful collaboration. We have data. We have natural history of the disease because of the patient registry.

And, again, we come with data and we come with experience and we come with the networks that can make these things happen.

So I just gave you an example. That was the example.

Mr. Pallone. No. That is fine.

We are hearing a lot about the various expedited drug review processes at FDA, and it is clearly a push by many to get the Agency to use these pathways more frequently and in more disease areas. And I share the goal of speeding the therapies to patient at the earliest possible time.

But I think we need to be cognizant of the risks that could accompany that speed, and we especially need to be concerned about such risks if we are ultimately thinking about somehow requiring more frequent use of these expedited pathways through legislation. And I know you share that concern.

Your testimony mentions the health risk that could result from approving therapies based on early data that needs more vigorous study, but you also describe the possibility that these kinds of approvals could endanger progress toward the development of other treatments.

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Can you just elaborate on both of those concerns, if you would.

Mr. Beall. Well, certainly, one of the things when you are dealing with a small population -- and now we are talking about personalized medicine where you may only have 25 patients with a certain genotype that may be approachable or therapeutic opportunities for that particular drug -- if those patients were introduced to a drug that was less than effective, what happens when the next drug that could be effective -- how do you do the clinical trial?

So I think that is really very critical because we want to make sure that our first introduction is drugs that are efficacious, and then we move forward to the next level. Because then you really are depriving, if you don't have safe drugs, of developing good drugs and effective drugs that could move us above the therapeutic options that we have.

So I think that that is the critical thing that we always face. There is always the risk. But now we are dealing with small populations, personalized medicine. Maybe there is only going to be 6, 10, 1,000 patients.

So I think you have to be particularly critical on that issue with rare diseases.

Mr. Pallone. Okay. Yeah. I just wanted to echo another point you made in your testimony about the importance of resources.

And I couldn't agree more, that, as you say, FDA needs resources

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to ensure that they can rely on the best regulatory science available and they need adequate resources to enable them to -- you know, basically to meaningfully engage with the patient community.

And, you know, we have this 21st Century Cures Initiative, which is progressing now. We have had some sort of larger meetings and now some hearings. And my colleagues always ask, you know, what can Congress do.

And I think that the most effective thing we can do is provide adequate resources to make sure that FDA, as well as NIH, have the resources to fulfill the expectations we have for both agencies.

And I know -- I hear not only from the agencies, but, also, from my constituents, that, you know, they don't have enough resources. So I think that is -- I just wanted to echo again what you said.

Thank you, Mr. Chairman.

Mr. Pitts. The chair thanks the gentleman.

I now recognize the vice chairman of the subcommittee Dr. Burgess, 5 minutes for questions.

Dr. Burgess. Just before my time starts to run, could I make a unanimous consent request?

Mr. Pitts. You may proceed.

Dr. Burgess. I would like to move that the committee make people aware that, if someone wishes to contact or communicate with the Cures Initiative, it is cures@mail.house.gov.

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I know there are many people watching who think, "I would like to interact with the committee staff." So that is the way to do it.

Mr. Pitts. Thank you.

Without objection, so ordered.

Dr. Burgess. Very well. I knew they wouldn't deny me.

Let me ask Ms. Furlong. You were kind enough to mention the work on the MD CARE Act, and thank you for that. As you know, we will likely be marking that up next week. So that is a big milestone.

Can you talk about how the MD CARE Act needs updating and the type of updating that this committee has pursued.

Ms. Furlong. Certainly. And thank you for the question, Dr. Burgess.

The MD CARE Act was the solid foundation that set Duchenne and the muscular dystrophies -- really galvanized their progress.

So the MD CARE Act was passed -- enacted in 2001 and reauthorized in 2008. And right now the amendments are really to look at what we have learned in the meantime.

So the cardio -- the cardiac issues in Duchenne muscular dystrophy are real and they have to be tackled in order to answer the question. As you look at these therapies that -- potential therapies that were hopeful to be approved in the next months and years, they extend function. Will they protect or have a negative effect on the heart?

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So it is the gaps that we need to really look at with the amendments, in addition to the fact that, when this legislation was enacted in 2001, young boys with Duchenne didn't live to be adults.

So now we have an adult population and we need to really address those adults in terms of their medical care and, also, to incentivize and understand how to treat them, how to encourage them to have long and independent lives as they become adults and reach for their dreams.

So I think that the MD CARE Act is now looking with the muscular dystrophy committee from the NIH and other agencies. Their research plan has to be updated and these amendments to be incorporates so that we are really achieving the full effect that the MD CARE Act was initiated for.

Dr. Burgess. Thank you.

And, of course, Mr. Beall will also acknowledge that the population of patients is changing because of some of the successes that has happened over the past several years.

And in both of those illnesses, both cystic fibrosis and muscular dystrophy, it is important that we keep pace with the way the patient population is changing.

We want people to live longer and fuller lives with their conditions and, at the same time, we don't want the legislation then to stymie that. So it is, in my opinion, an important step forward.

Dr. Beall, we talked -- or you talked about the development of

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mutation-specific therapies and the next evolution in precision medicine and you could see the cystic fibrosis example impacting the way we address other serious illnesses.

Is there something more you would like to add to that?

Mr. Beall. Well, again, we are clearly in the age of personalized medicine. I mean, fortunately, with the completion of the human genome, we understand the genetics of so many more diseases and genetic diseases that it is a very critical time for us.

Mr. Pitts. Microphone.

Mr. Beall. Not on? Okay.

I just saw Dr. Collins downstairs, and he is excited about -- because he was one of the discoverers of our CF gene.

So we live in a very unique age, and I think more and more therapies are going to be directed towards specific mutations.

And that is one of the reasons that we have to have these kinds of patient registries, so we can start to identify those mutations.

When Vertex felt that they had a drug that might work on a certain mutation, the small drug that came out, G551D, we were willing -- we were able to tell them in the United States we have 1,100 of those patients within 5 minutes after they asked us because of a patient registry, because we have a documented history of the disease.

So I think that is why it is very important to have personalized medicine, therapies and the options for that, but it is also -- we have

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to be able to document the patients that can participate in the trials.

Dr. Burgess. Yeah. It is very powerful.

And, of course, you referenced to the 1965 registry. In 1965, you didn't know that we were going to know about the sequence of the human genome 30 years later.

Mr. Beall. Well, but we have been able to document it. Today we cover -- have 26,000 patients whose data is provided to our patient registry every single year.

Dr. Burgess. Let me ask you question. I am going to run out of time pretty quickly. But -- and this is either for Mr. Beall or Mr. Pops.

You know, the world is different now and you have people that are perhaps lucky enough to enter into a clinical trial and they are likely to, you know, perhaps have friends with the same condition.

So in the old days, a randomized clinical trial, you wouldn't know which arm to which you were randomized, who was getting the target or study drug, who was getting either an older therapy or no therapy. But now people communicate. Facebook. Twitter. They are likely to be Facebook friends.

How is that going to impact the ability to have a blind and randomized clinical trial? Are people likely to communicate with each other, I mean, look, "I am getting a lot better on this stuff. How about you?" "Wait a minute. I haven't seen a darn thing"?

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Mr. Pops. I think it is a real question. It is a real issue because -- and you can't pretend that it is not going to happen.

This is already happening, particularly as you get large cohorts of patients in randomized studies in multiple countries. They are all communicating.

So I think it is very important that we be really rigorous in maintaining the blind to the extent that we can.

Dr. Burgess. To the extent that we can. But, also, we probably need to embrace the fact that the information is out there and being communicated and, to the extent that it can further enhance what we are doing --

Mr. Pops. So let's take advantage of it.

Dr. Burgess. Yes.

Mr. Pops. Let's do more in the aftermarket. Let's approve drugs and collect this information and get a more nuanced view of the drugs' use in the real world and turn it to our advantage.

Mr. Beall. And, in some cases, it is going to make it easier to do clinical trials when you can have large networks that exist out there, when they can report patient-reported outcomes and things like that.

So I think it is -- sometimes it is looked at as a disadvantage, but we ought to turn it -- as Mr. Pops just said, we ought to turn it to an advantage because I think it can expedite the ability to do

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clinical trials as we move forward with the technology.

Dr. Burgess. Great. Thank you.

Ms. Furlong. And it should expedite post-hoc analysis so that we can see the long-term effects. Because in a clinical trial of 12 months, for instance, or -- plus or minus, you might not see the full effect of a drug that is multisystemic. So it will enable us to understand the full impact on the patients' lives.

Dr. Burgess. Thank you, Mr. Chairman. I yield back.

Mr. Pitts. The chair thanks the gentleman.

Now recognize the gentlelady from Illinois, Ms. Schakowsky, 5 minutes for questions.

Ms. Schakowsky. Thank you very much.

I had a question for Dr. Lichtenfeld -- actually, for anyone on the panel that wants to comment on this.

This is about quality-of-life outcomes. I mean, obviously, if this is a known life-threatening disease, you want to do everything you can to make sure that the therapies match the disease.

But there are -- you would say, when these quality-of-life outcomes are rigorously measured and supported by the FDA, they can and should be included in drugs' labeling and can by themselves be a basis for a drug's approval.

I certainly know people who have suffered so much from side effects of drugs. And I just wonder, in the whole process of drug

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approvals, how much are these quality-of-life issues really looked at? As a basis for approval or just as a basis of whether or not they are used?

Dr. Lichtenfeld. Thank you for your question.

In fact, it is a work in progress. Let's understand that quality of life is a buzzword today, but it wasn't a buzzword very recently.

So as we look at the issues, shall we say, of palliative care, of supportive care, quality of life, issues that the American Cancer Society and many others have been involved in, it is relatively new to the table.

Having said that, there have been issues recently with a drug -- one particular drug where, had the question really centered around was the -- even though the drug may not have met the FDA standard -- and this was about 2 years ago -- even though it had not met the FDA standard, did it meet the quality-of-life standard? Did it improve the quality of life of the -- it happened to be a breast cancer drug -- for the women who took it?

Because that would have been an important consideration. And, unfortunately, the quality of the data measuring quality of life was inadequate.

So going forward -- I mean, cancer patients have enough on their plates, as do everyone represented at this table, as do patients throughout this country. We need to be aware that quality of life is

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an important part of the treatment process, and we need to have tools in place.

They are not uniform yet. They are not as good as we would like. But they have to be in place to measure quality of life, and that has to be considered. And patient-reported outcomes are very much a part of that process.

Ms. Schakowsky. Yes. Go ahead, Doctor.

Mr. Pops. I just wanted to make a comment as it relates to patients with chronic disease as well. We talked a lot about cancer and orphan, small diseases.

We work in the field of chronic disease -- schizophrenia, depression, addiction -- where patients are taking medicines for long, long periods of time.

And simple things that may seem prosaic to the researcher, like nausea --

Ms. Schakowsky. Sure.

Mr. Pops. -- fatigue, propensity to get addicted or dependent on the drug, these are really important inputs that we want to hear from patients about.

Ms. Schakowsky. And is that part of the process?

Mr. Pops. It is less part of the approval process today than I think it will be in the future. It is certainly part of the utilization process as patients make a determination, "Which medicine do I want

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to stay on for years and months?" I think that is a critical part of it, but it is not really incorporated in the consideration of the approval.

Ms. Schakowsky. Especially where all things might be equal in effectiveness, whether or not something causes nausea, fatigue, could be really important.

Mr. Pops. That is right. Particularly if you are launching a new medicine into a large category where there might be an abundance of generic drugs that are safe and effective, but might not hit all of those parameters for certain subsets of patients for long periods of time.

And we just want people to be sensitive to the fact that, from the patient perspective, there are differences between the medicines.

Ms. Schakowsky. Right.

And then, also, Dr. Lichtenfeld, I wanted to ask you about small-sized trials. And you mentioned one of the drawbacks.

I had talked about the extent to which women aren't considered. And I would just be concerned -- I understand the plus. I do. But if we rely too heavily on them, isn't there the real risk of excluding important populations?

Dr. Lichtenfeld. Well, the answer is yes, there is a real risk of excluding important populations.

In fact, when you talked about women and heart disease, I remember

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back in the early 1990s when the article came out talking about the absence of women in clinical trials for the treatment of hypertension and heart disease. So this is an issue I am aware of.

But let's talk about the other side of the coin, and that is, when you are sitting -- I have sat in the presentations at ASCO, at oncology meetings -- and you see a presentation of 80 patients and you see what we call waterfall plots -- basically, the responses in survival that occur -- and suddenly, you know, 70 percent of those patients are having significant responses, I don't think -- in a disease where there was no treatment before, I don't think one asks the question -- I mean, they ask the question in followup, but not at the moment.

And what has happened and what has been exciting to me is I am now sitting in those presentations every June and I see -- I actually -- I wrote about it -- it took a year for one of the drugs to go from clinical trial to approval because it was that effective in the disease where there was no other treatment available. That is pretty spectacular. That is new thinking. That is a new approach.

Now, we have learned more as time has gone on. Yes. Doesn't mean we have stopped learning, as was mentioned before about cystic fibrosis. But when you suddenly see moments like that, no one would want to hold back. Develop the data, yes, but don't hold back the opportunity.

In fact, even a phase 1 trial that was presented at this ASCO

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meeting in June, the company, actually -- well, not the company, but ASCO in the press release indicated the company was willing after a phase 1 trial to put it into compassionate use. And that is pretty -- again, pretty amazing, a major change in the way that traditionally we have seen cancer drugs move through the pipeline.

Ms. Schakowsky. Thank you.

I have overstayed my time. Thank you.

Mr. Pitts. Sure. Thanks to the gentlelady.

Now recognize the gentleman from Virginia, Mr. Griffith,
5 minutes for questions.

Mr. Griffith. Dr. Lichtenfeld, let's pick up there, because I think that that compassionate use is something that -- we really need to be figuring out how we can make it more effective and how we can do it faster at the Federal level.

You talked about in your testimony that patients needed to be involved both on saying, you know, they had -- what kind of nausea they had and what the pain levels were and so forth, and I agree with that.

But I also think that, particularly when you have no treatment, that patients need to be involved in that, too. And as Ms. Furlong said earlier, when there isn't a treatment, you are much more willing to take those risks than you would be if there is some other treatment out there that might work, but this might be a little more comfortable.

And I want to give both you and Ms. Furlong an opportunity just

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to address that further.

Dr. Lichtenfeld. Well, thank you. And I appreciate the question, and I know you mentioned it earlier.

It is a complex issue. It is not a new issue. As you may well be aware, it has been around for some time with the number of drugs that have gone through the pipeline, which seem to show some opportunities. There are substantial -- and I also know it is under -- various state legislatures are involved.

And I am sitting here today both as a representative of the Society, but also as an individual, and understand that there are discussions on both sides of that issue and they are complicated.

Bottom line is that we need to understand what drugs work when they work. We need to understand that patients need to have access to promising drugs as soon as possible.

Companies make those decisions as to how they are going to handle that process. The FDA, as a matter of fact, has approved almost all of the applications they received. And we need to have those discussions to come to a better resolution about how to address that issue.

Mr. Griffith. Well -- and what I would say is that whatever we can do -- I think I speak for a lot of the members of the committee -- I am probably a little more out there than some -- but whatever we can do to help by changing the law to expedite that process, we will do.

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Dr. Lichtenfeld. We would be glad to have those discussions on behalf of the Society, sir.

Mr. Griffith. Ms. Furlong, did you want to make another comment about risk assessment? Because, obviously, when your boys were sick, you probably would have taken anything that had any promise of hope.

Ms. Furlong. I think I could tell you stories about looking in China to see some tea that you might be appalled about, but that was long ago.

I think this also -- it really is up to the companies. FDA has always, to my knowledge, at least in the Duchenne and other fields, been willing to entertain and talk about compassionate use.

I think for the rare-disease community this really talks about and gets us back to trial design.

In general, trials are designed for -- to test a small subset of patients. In the Duchenne community, the 6-minute walk test is the standard outcome, primary outcome measure.

So that means, as a child with Duchenne, you have to walk 6 minutes and even further, as we learn more about the testing. It is a very narrow subset of people within a certain framework of that 6-minute walk test, which, as you can imagine, leaves a great number of people outside the trial.

So I think trials have to be designed that are inclusive and welcoming of people that live with the spectrum of the illness, both

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very young as well as adults with very limited functional ability.

That way, we can test those in those populations. We can have labels that are broad and then provide access to all. So I think that might be a better solution.

Mr. Griffith. Thank you.

I look forward to working with you all.

And, with that, I yield the remainder of my time to Dr. Burgess.

Dr. Burgess. I thank the gentleman.

Dr. Lichtenfeld, I just wanted to follow up with you because your specialty has been involved in this type of activity probably longer than any other branch of clinical medicine, going back to 1955 when the developmental therapeutics program was put into place at the National Cancer Institute.

So with that breadth of experience within your specialty, are there things that you want to share with others about what that experience has taught you?

Dr. Lichtenfeld. Well, what we did back in 1965 or whenever was a lot different than what we are doing today. I don't want to take the time to really go into it. You may be aware of it.

But here is the message. It didn't happen overnight. It took 40 years of research to get us to the tipping point where we understood the genome and had the opportunity to take advantage of that and move forward.

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Immunotherapy, the same story. It has taken us 40 years. That was a substantial amount -- I don't want to underestimate the value of research investment to get us to the point where we are, where suddenly we look like we have so much to offer and to do.

I also comment, with regard to my co-panelists, that they have populations and they have demonstrated that finding the patients where they are is critically important.

We have a substantial amount of work to do to understand not only the clinical trial mechanism, but also the medical practice system, so we can make sure that patients and communities -- I live in a small town in south Georgia -- that my friends have opportunities to get these drugs in clinical trials and be part of that process. There is a lot of work to do.

Dr. Burgess. Thank you, Mr. Chairman. I yield back.

Mr. Pitts. The chair thanks the gentleman.

Now recognize the gentleman from New York, Mr. Engel, 5 minutes for questions.

Mr. Engel. Thank you, Mr. Chairman and Mr. Pallone, for holding this hearing. I am pleased to have this opportunity to further consider how patient perspectives can best be incorporated into the therapeutic development process.

As the author of the ALS Registry Act and the Paul D. Wellstone Muscular Dystrophy Community Assistance Research Education Amendments

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of 2008 and 2013, along with my colleague, Dr. Burgess, I have worked to be a voice with those with rare and orphan diseases.

I am encouraged by the advances we have made into the causes and mechanisms of these diseases, as well as our progress toward treatments, but, obviously, we still have a long way to go.

One of the most striking gains we have made is for individuals with Duchenne muscular dystrophy. As Ms. Furlong mentioned, our efforts have added an average of 10 years to the life expectancy of boys with Duchenne. And now, as life expectancy increases, we face new challenges in finding effective therapies.

The patient community brings an important perspective and understanding to this process, and I am interested to see how we can best use that knowledge to assist medical researchers with therapy developments.

So, Ms. Furlong, let me ask you this. I am particularly interested in the way the Duchenne patient community is engaged with the FDA to help inform the benefit-risk determinations made by agency reviewers, as well as the Duchenne community guidance document you referred to in your prepared testimony.

Could you please comment on how you hope to see these efforts affect the therapeutic pipeline and the various stakeholders who are part of that pipeline.

Ms. Furlong. Yes. Thank you, Mr. Engel, for the question.

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The benefit-risk really originated out of discussions with the FDA because, in our discussions -- early discussions, it was known that we were telling anecdotal stories that the equation of benefit-risk was different in, for instance, Duchenne muscular dystrophy than perhaps some more common disease.

And in that the FDA suggested to us that they agreed, but they didn't have anything they could rely on, any quantified evidence-based document that could help them make those decisions.

So we agreed to go out on benefit-risk and did the pilot with 120 parents. We learned that their priority is disease stabilization and they were willing to accept a great deal of risk. In fact, they are living with a great deal of risk, as they know that their child has a fatal illness.

So the FDA has now asked us to expand that study to a greater number of patients than 120 patients and, also, to ask these questions of the young men with Duchenne. Our hope is that they will incorporate it into the review process and they will give -- they will demonstrate to us how and when they use it and when they don't and what makes sense for them as they make their decisions.

Mr. Engel. Thank you. And thank you for your advocacy and hard work. It is very much appreciated.

Dr. Summar, can you talk about the role you think the patient perspectives should play in developing therapies for diseases like ALS

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and muscular dystrophy that have limited treatment options and for which quality of life is, obviously, an especially important factor to patients.

How can the FDA best consider the views of patients and families when examining the benefit-risk calculus for these diseases?

Dr. Summar. Thank you for that question, Mr. Engel.

This really kind of expands across the entire field of rare diseases, but your question is particularly relevant for those two groups.

Patients often tell us about things that they wish were better that we never thought of. One of the things I have run across time and time again is, when we go and ask our patients, "What is the worst part of this disease?" -- a lot of times it is parents in the case of pediatric patients -- they will list some things. And sometimes the things we thought were most important are number nine or ten on the list.

So I think, when we look at what our therapeutic targets are, what our quality-of-life targets are for these diseases, patient and family input is a huge factor, and I think it is something we can incorporate a lot better than we have.

I think during the early stages, particularly when we are designing our pivotal trials, clinical trials, looking at what end points are -- I think that those are going to become more and more

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important.

And the other thing, of course, is the small group sizes with these. Many times it is hard to pick one single outcome variable that you are going to be able to achieve.

The smallest study I have been involved with is was five patients for an approval process. Getting one exact target for that -- fortunately, the effect of the drug was massive; so, we were able to do it. But if it had been a -- milder, I might have needed more than one outcome variable.

So I think families can help us determine what is important there. They can help us, also, as we talked about with some of what risk is tolerable in those situations. It is different. And there are 7,000 different rare diseases. Each one of these is unique in its own regard. But there are some commonalities like that.

Mr. Engel. Well, thank you. And thank you for your comments, and also thank you for your interest.

And I want to thank the panel for a very interesting discussion.

Thank you, Mr. Chairman.

Mr. Pitts. The chair thanks the gentleman.

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

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

And I thank the panel for their testimony today.

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I know we have been talking about this and you have had an opportunity. I want to give you more of an opportunity to respond on this.

On Wednesday, I asked one of the witnesses about his statement in including patients in the clinical trial process, but I want to make sure that you all have every opportunity to respond to this.

If patients had a greater role in clinical trial design -- and I know you have touched upon this -- if trials measured qualitative data from patients like, "How do you feel?", "Is it less painful?", what have you, how would things be different? And what would you like to see?

We will start with the --

Mr. Beall. I would like to start.

First of all, the patient-reported outcomes I think has been part of every clinical trial in cystic fibrosis for the last 10 or 15 years. Some of the tools are not the best at this point, but we are working to refine them.

We have just spent as a Foundation a large effort to look at the patient-reported outcomes as a kind of specific validated tool for CF, and it is going to be submitted to the FDA and go through a validation process. In the past, we have used one that was generally for lung disease, but it may not be specific.

So this is a science that is evolving. I mean, you know, a decade

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ago or 15 years ago, 20 years ago, PROs were not really incorporated.

So it is a science that is evolving, and it has to be evolved with -- not only with the FDA, it has to be evolved with the sponsors, too, because they have got to be willing to incorporate those into the clinical-trial process.

So I am encouraged by the process, but I will tell you the -- just in this last trial we had where their lung function went up and the exacerbations went down, we didn't have a statistically significant improvement in the patient-reported outcomes.

Because we are treating a -- when you are starting to treat the basic defect, you are treating the whole disease process and you are looking at extending lives.

And the patients may not feel that from day to day, but over years, you may have a tremendous impact on those patients. So it is a tool that can be used, but it shouldn't be used exclusively.

Mr. Bilirakis. Thank you very much.

Ms. Furlong, do you have a response?

Ms. Furlong. Sure.

So I agree with Dr. Beall. And patient-reported outcomes are incredibly important, but I think this is where involving the patients in the design and conduct of clinical trials is really going to be important.

Because, for instance, how do we measure energy and endurance?

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How do we know that turning over in bed is important to patients as opposed to an outcome measure such as the 6-minute walk test?

So I think things are important to patients that have a real effect on their lives. For instance, as you can imagine, if a boy can still text at the age of 18, that gives him independence. If a child can walk up a single step, they can enter buildings. If a child can roll over in bed, that makes the families' quality of life overall, in general, much, much better.

So I think the use of patient-reported outcomes and including the patient voice in the discussion about what the clinical trial looks like and what the measurements are, both primary and secondary, is going to be incredibly important.

Mr. Bilirakis. Thank you so much.

Mr. Pops, do you have a comment or --

Mr. Pops. I think these outcomes are so critical. In the world that we are developing drugs in, which is in psychiatry often, in schizophrenia, depression, addiction, the end point of the clinical trial -- the hard end point is asking people essentially how they feel.

And so how you feel is typically embodied in the set of validated scales, but those often don't capture some of the most important parts of how they actually feel over time.

A perfect example might be an opioid dependence or an alcohol dependence, where a critical question the patients ask us when they

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take our medicine is, "Is my craving going to go down? Am I going to crave this less? It may block the receptor and keep me from drinking, but is my craving going to change?"

That was not a validated end point. That was something we couldn't incorporate in the label, but it is essential to the patient's perception of the disease.

Mr. Bilirakis. Good point.

Doctor?

Dr. Lichtenfeld. About 4 weeks ago at ASCO, the oncology meeting, they showed a picture of a lady who was 96 years old who had received a phase 1 drug -- that in itself is a fascinating point -- whose cancer completely resolved.

And on the bottom end of the before and after picture -- on the after picture, you saw a trace of a little smile. And I noticed that smile and I tweeted it, actually. I took a picture and tweeted it and it got re-tweeted quite a bit. And then the lecturer said, "Yes. That really is a smile" in front of 2,000 people.

What I am trying to say is -- by that example is that is what we have to -- we have to be able to measure and aggregate in a scientific way to show that the treatments make a difference.

One example of one lady in an unusual situation, but something that I think all of us agree -- I would echo the comments that were already made -- is so critical to understanding and -- particularly

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in the oncology world, what we do and how we do it and the goal that we have to have of improving quality of life.

Mr. Bilirakis. Thank you.

Dr. Summar?

Dr. Summar. Yeah. I will just use another example, too.

We had a new medication we were looking at. Most of the patients with rare diseases are on the medicines they take for life. So it is every day, day in and day out. And these care plans are often complex and highly -- they really affect the whole family.

So the new drug looked like it was promising from the standpoint of, you know, maybe a little bit better efficacy, a little bit better control, but it was five times a day instead of two or three times a day compared to the old one.

And the families were like, "Why would we add three more times a day of dosing for the small effect?" And no one had really bothered to ask them that before we started.

So I think there is all of these things that really getting the patient input early on is going to make a difference.

Mr. Bilirakis. Thank you so much. Appreciate it.

Mr. Chairman, can I ask one more question?

Mr. Pitts. You may proceed.

Mr. Bilirakis. Okay. Thank you so much. Appreciate it.

Dr. Beall, the CF Foundation's venture philanthropy model has

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produced incredible results. Congratulations. Your foundation found your breakthrough drug when it helped translate some of the early research through the valley of death, and now you have the Kalydeco. It sounds similar -- I am sorry.

How are you able to establish this program? And how can other groups adopt this similar model?

Mr. Beall. Well, it is a willingness to take risks. That is what you have to do in drug discovery. And we were frustrated by the fact that companies were not getting involved in the orphan diseases.

So the whole concept here was to say, "Take some of the risk out of biotech companies or pharmaceutical companies to get engaged in CF research." And, as I said, we spent \$42 million initially to start a high-throughput screening that led to Kalydeco.

I think what is the most important and gratifying thing for the Cystic Fibrosis Foundation -- and I know Ms. Furlong was in my office a number of years ago -- and it is the ability -- and what we are seeing is so many other organizations are feeling the same impatience that our foundation felt 14 years ago in adopting this.

One of the first times I talked about venture philanthropy at the bio meetings, we had 10 people in the audience. And now it is really becoming really inherent in what many voluntary health organizations are doing.

In fact, FasterCures has been an organization that has been

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central to making some of that happen. There are law firms that specialize in it.

So we love to share our ideas. We share our ideas all the time. And it has been very gratifying to our community that we happen to be fortunate enough to be able to start it because we had the resources. Bill and Melinda Gates gave us \$20 million to start our program. We had other dollars to really make that initial investment.

Mr. Bilirakis. Can you tell us how you established -- again, successfully established the registry.

Mr. Beall. As I say, it goes back a long time. But, you know, Dr. Zerhouni was here a number of -- several years ago when he was the head of the NIH, and he says one thing about the CF community, it is a community with a culture of research.

And every patient who goes to see -- or goes to one of our care centers is asked, "Do you want to participate in a patient registry?" And I think it is 99.5 percent of the patients that say, "Yes, I do" and then signs the informed consent.

So it is all part of the culture. It is part of the culture the organization creates. It is the physicians and it is the relationships and the recognition that it is an important part of having a disease because we can't cure this disease without their involvement.

Mr. Bilirakis. Very good. Thank you very much. Appreciate it.

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I yield back, Mr. Chairman.

Mr. Pitts. The chair thanks the gentleman.

Dr. Summar, I didn't get to you in my round.

On Wednesday, we heard an idea thrown out there that, you know, there are vast amounts of data available that are not being utilized. And we all know what an organ donor is. The idea was that we have data donors.

Now, how would this play -- and you mentioned the IRB system, the risk enterprise. What is your reaction to that?

Dr. Summar. This is something we talk about when we are having coffee a lot.

There are data sets all over the place. In fact, most of them end up usually lost when someone's computer gets recycled. I have -- we had a physician lose, you know, 15 years of data because his Excel spreadsheet didn't update.

I think a way -- find a way that balances, obviously, people's desire for confidentiality versus the irreplaceable and oftentimes irreproducible amounts of data that are out there. We really do need to find that balance.

My reaction to that would be I would love to find a way forward with that. That one is going to -- you can see a lot of sides to that question. But I definitely think it is worth looking at.

And I think what we find is a lot of patients are like, "Yeah.

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I will put it out there. I am fine with that." There will be a small core that won't. You can take a count for that. But I think most folks, if you ask them, saying, "Would you feel okay if your is data out there so everybody can take a look at it?" would be fine.

You see people opening up their genomes, who had their genomes sequenced, saying, "I will publicly post it along with my medical health history." A lot of folks want to help.

Mr. Pitts. Thank you. Thank you.

Dr. Burgess. I did that. We did that. I mean, that is a real thing that is happening right now. And, yeah, privacy is something we all value, but it also is a voluntary relinquishing of a portion of that for the greater good.

I think that is something we ought to not encourage -- well, not encourage, but we certainly shouldn't stand in the way if that is an activity that --

Dr. Summar. Right.

Dr. Burgess. And, unfortunately, I can't say that we don't always respect that, that we shouldn't stand in the way. But -- enough about that.

Mr. Pitts. All right. The chair thanks the gentleman.

That concludes the questions of the Members who are here. Another exciting, informative, very important hearing. Thank you so much for coming.

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Members will have followup questions, and we will send those to you. We ask that you please respond promptly. I remind Members they have 10 business days to submit questions for the record, and that means Members should submit their questions by the close of business on Friday, July 25th.

[The information follows:]

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Mr. Pitts. I have a UC request, a statement for the record, from the National Health Council. Without objection, that will be inserted into the record.

[The information follows:]

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Mr. Pitts. Without objection, the subcommittee is adjourned.

[Whereupon, at 12:19 p.m., the subcommittee was adjourned.]