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21ST CENTURY CURES: THE PRESIDENT'S COUNCIL OF ADVISORS ON SCIENCE AND TECHNOLOGY (PCAST) REPORT ON DRUG INNOVATION

TUESDAY, MAY 20, 2014

House of Representatives,

Subcommittee on Health

Committee on Energy and Commerce

Washington, D.C.

The Subcommittee met, pursuant to call, at 10:00 a.m., in Room 2322 of the Rayburn House Office Building, Hon. Joe Pitts [Chairman of the Subcommittee] presiding.

Members present: Representatives Pitts, Burgess, Shimkus, Blackburn, McMorris Rodgers, Lance, Cassidy, Griffith, Bilirakis, Ellmers, Barton, Upton (ex officio),

Pallone, Engel, Schakowsky, Green, Barrow, Sarbanes, Waxman (ex officio), and DeGette.

Staff present: Clay Alspach, Chief Counsel, Health; Gary Andres, Staff Director; Mike Bloomquist, General Counsel; Matt Bravo, Professional Staff Member; Noelle Clemente, Press Secretary; Paul Edattel, Professional Staff Member, Health; Sydne Harwick, Legislative Clerk; Robert Horne, Professional Staff Member, Health; Carly McWilliams, Professional Staff Member, Health; Katie Novaria, Professional Staff Member, Health; Krista Rosenthall, Counsel to Chairman Emeritus; Chris Sarley, Policy Coordinator, Environment and Economy; Heidi Stirrup, Health Policy Coordinator; John Stone, Counsel, Health; Ziky Ababiya, Democratic Staff Assistant; Phil Barnett, Democratic Staff Director; Eric Flamm, Democratic FDA Detailee; Elizabeth Letter, Democratic Press Secretary; Karen Lightfoot, Democratic Communications Director and Senior Policy Advisor; Karen Nelson, Democratic Deputy Committee Staff Director for Health; Anne Morris Reid, Democratic Senior Professional Staff Member; and Rachel Sher, Democratic Senior Counsel.

Mr. {Pitts.} The subcommittee will come to order. The chair will recognize himself for an opening statement.

Today's hearing relates to the 21st Century Cures Initiative announced by the Energy and Commerce Committee on April 30, 2014. This Cures effort is envisioned to explore ways to accelerate the discovery, development and delivery cycle for new medical breakthroughs. Through this effort, Congress hopes to clear a path to find more cures and treatments, while also creating jobs, and keeping America as the innovation center of the world.

Shortly following the announcement of the Cures Initiative, the committee issued a white paper on May 1, 2014, entitled 21st Century Cures: Call for Action, which more fully discusses the ideas behind the Cures project and issues of call to action, call for ideas. The first goal of this project is to solicit ideas. Congress does not have all the answers, but we do have a role to play in ensuring our nation's laws and regulations, keep pace and compliment the biomedical research and innovation that is happening at lightning speed.

Earlier this month, we heard from the NIH, FDA, patient advocates, university leaders, and other scientific pioneers about their ideas, challenges and successes. Today, we will hear from experts who contributed to the President's Council of Advisor on Science and Technology, PCAST, report on propelling innovation in drug discovery, development and evaluation. This important report hits on a number of topics that we will have to explore if we are to truly advance Cures. These ideas include, among others, making sure incentives are in place to ensure capital is flowing towards research and development of new cures, and designing clinical trials to the appropriate size and scale, given the growth of targeted personalized medicine.

Today, we hope to learn more about these proposals and others put forth by PCAST, and determine which ideas or recommendations could potentially advance the 21st Century Cures Initiative.

Excitingly, the fight for faster cures in the 21st Century will not only foster medical innovations, but it can also make our healthcare system more efficient, and can save lives.

I want to welcome our witnesses today. I look forward to hearing--learning more about the advancements in biomedical research and innovation.

[The prepared statement of Mr. Pitts follows:]

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Mr. {Pitts.} And I ask for unanimous consent to include the following statements for today's hearing record from Dr. Raymond Woosley, former president of the Critical Path Institute, and one of the experts that participated in the development of the PCAST report, and Dr. Janet Woodcock, Director of FDA Center for Drug Evaluation Research Blog Post, ``Progress on the 2012 Drug Innovation report by PCAST'' from May 20, 2014.

Without objection, so ordered.

[The information follows:]

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Mr. {Pitts.} Thank you. I yield the remainder of my time to Dr. Burgess.

Dr. {Burgess.} Thank you, Mr. Chairman. Thank you for yielding. Thank you for having this hearing, and especially thanks to the chairman and ranking member of the full committee for pursuing the 21st Century Cures Agenda.

So this is an accompanying bipartisan effort to listen to you, the scientists, to listen to doctors, listen to researchers, listen to patients, and, yes, we will listen to government agencies to find out how we can continue to lead the world in scientific discovery that ultimately leads to cures, treatments, medical devices that will improve human health, and, most importantly, alleviate human suffering.

In September 2012, the President's Council of Advisors on Science and Technology issued a report to the President on propelling innovation in drug discovery, development and evaluation. The report provided recommendations on how to ensure we are doing everything we can to capture the significant amount of knowledge that has been gained in the last few decades, and to ensure that the knowledge is

translated into cures and actually make it into the lives of patients. The report found many of the same themes that we have heard for the last 10 years in this committee. While our scientific knowledge has significantly grown, the promise of that knowledge has not been realized. The recommendations of the President's council also mirror familiar suggestions, including building off existing authorities to accelerate therapeutics and ensure management of regulatory agencies appropriately balances the benefits and risk. With this-- when this effort was launched, we said we wanted to hear from everyone, and I am pleased that we are evaluating the advice that is being given to the President in this area.

I certainly look forward to this hearing. I look forward to your testimony. I look forward to all of the participation of our witnesses.

Thank you, Mr. Chairman. I will yield back.

[The prepared statement of Dr. Burgess follows:]

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Mr. {Pitts.} The chair thanks the gentleman.

Now recognize the Ranking Member, Mr. Pallone, 5 minutes for an opening statement.

Mr. {Pallone.} Thank you, Chairman Pitts, and thank you for calling this hearing.

I wanted to initially ask unanimous consent to enter into the record a--an article on the progress of the 2012 Drug Innovation report by PCAST, if I could. I believe you have it, Mr. Chairman.

Mr. {Pitts.} Yeah, we just did that.

Mr. {Pallone.} All right, thank you.

Let me also thank Chairman Upton for convening the 21st Century Cures Initiative, and also Ms. DeGette, who was very much involved with that.

We all agree that the Federal Government and Congress can play a role to help accelerate the discovery, development and delivery of promising new treatments to patients, and the question remains how to best advance those goals. I look forward to engaging this process as we meet with stakeholders, and gather ideas and input from experts on

what, if any, policies Congress can consider moving forward. And most importantly, I look forward to working with my colleagues in a bipartisan way to ensure that promising new medicines get to patients in a timely manner, and they are safe and effective.

The committee already has a great record on that effort, most recently with the passage of the FDA Safety and Innovation Act of 2012, or FDASIA. That law reformed and revitalized many FDA programs to improve its regulatory scheme, to facilitate a more efficient and predictable review process. Specifically, we updated the regulatory pathways under which FDA provides for expedited reviews of drugs. WE also aided for the first time the breakthrough therapy, Pathway, and all of these programs served a goal of helping drug sponsors and the FDA work together to cut development time.

In addition, I am currently working with Chairman Pitts on a Bill that would streamline the DEA's scheduling process as it relates to improved drug therapies. If we are going to have a comprehensive discussion about how to promote innovation and medical advancements, we can't simply focus on

the FDA. The work being done at NIH and through the country at research universities like my hometown school of Rutgers University, has to be properly funded. Discovering cures and developing effective treatments are complex, difficult and expensive endeavors. NIH is the premiere biomedical research institution in the world, and I hope this committee can find ways to ensure that NEH--NIH has the necessary tools to maintain that designation.

When we talk about the delivery of therapies, we have got to address access. Medical advances and cures at the earliest possible time is our shared goal, but we all must work together to ensure that when discovered, those cures can get to all patients, and not just those who can afford them.

So, Mr. Chairman, based on your comments and actions to date, I am hopeful we will have these conversations as we move forward. Today, the committee will examine the President's Council of Advisor on Science and Technology, or PCAST, Report on Drug Innovation. That report issued in September of 2012, only a couple of months following the passage of FDASIA, puts forth a number of proposals across a large spectrum of policies, from funding basic biomedical

research, to developing economic initiatives. And there are a number of ideas in this report, so I look forward to flushing out their relevance, and thank everyone for their input today in moving forward.

[The prepared statement of Mr. Pallone follows:]

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Mr. {Pallone.} And I have about a minute and a half. I would like to yield to my colleague from Texas, Mr. Green.

Mr. {Green.} Thank you to our ranking member and the chair for having this hearing, and our witnesses for testifying, and yielding the time.

I applaud the committee for its 21st Century Cures Initiative exam and what steps are needed to harness scientific knowledge, and accelerate the pace of the new Cures. The--in 2012, this committee took an important first step in addressing the lack of new drug development to treat drug-resistant infections. Our committee colleague, Congressman Gingrey, and I were the lead sponsors of that legislation, along with a number of other of our colleagues on the committee, but I fear our work is far from finished. According to the report recently by the WHO last month, the antibiotic crisis is bigger and more urgent than the AIDS epidemic of the 1980's, and without swift and significant action, the implications will be devastating. The Gain Act was an important step to address--addressing a lack of new drug development, but it must not be the last. Weekly

reports of new global threats and cases identified here at home are a start reminder our ability to meet this threat relies in no small part upon a robust pipeline and new therapies. PCAST scientists, physicians and global health leaders have sounded the alarm. We need new incentives and approaches to continue fighting drug-resistant bacteria that build on the--and build on the work of getting it started. It would be wrong to let this opportunity for action pass us by.

I urge the committee to address this crisis head-on, and encourage meaningful development of the antibiotic space. I stand ready to work with you to achieve the worthy goal, and we do not have a moment to waste.

And I yield back my time. Thank you.

[The prepared statement of Mr. Green follows:]

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Mr. {Pitts.} The chair thanks the gentleman.

Now recognize the Chairman of the Full Committee, Mr. Upton, 5 minutes for an opening statement.

The {Chairman.} Well, thank you, Mr. Chairman.

So today marks our first 21st Century Cures hearing at the Health Subcommittee. We launched this bipartisan initiative earlier this month with one primary goal: accelerate the pace of the discovery, development and delivery cycle so that we can get innovative new cures and treatments to patients more quickly.

Today, we continue this important conversation with several of the distinguished experts who contributed to the President's Council of Advisors on Science and Tech Report on Drug Innovation. The President, in soliciting recommendations on this very important topic, decided propelling drug innovation is a policy worthy of exploring and advancing, and I couldn't agree more.

In their report, the President's advisors found that the nation's biomedical innovation ecosystem is under significant stress, citing the patient--citing the patent cliff facing

the pharmaceutical industry, declining investment from venture capital, and decreasing research and development in critical area, including Alzheimer's. We have heard similar concern in our discussion with patients, innovators and thought leaders.

So in order to address these issues facing our biomedical innovation ecosystem, the experts who contributed to the report recommended closing scientific knowledge gaps, addressing inefficiencies in clinical trials, considering more economic initiatives to decrease investment--to increase investment, and encouraging even more innovation at the FDA. The President's advisors put forth the following goal for our nation. ``Double the current annual output of innovative new medicines for patients with important unmet medical needs, while increasing drug efficacy and safety, through industry academia and government working together to double the efficiency of drug development by decreasing clinical failure, clinical trial cost, time to market, and regulatory uncertainty.'' I know that we can all agree to join the President and his advisors to meet that goal.

As the President advisors so rightly said, we must work

together to achieve the goal. This has to be a collaborative effort.

The committee recently put out a call for feedback on the PCAST report. We also asked for input from our nation's patients on the discovery of treatment and cures for their diseases. The 21st Century Cures Initiative ultimately touches everybody, every family, patients, doctors, loved ones, researchers, thought leaders, everyone, and we want input from all of those involved. Folks can email their ideas to Cures@mail.house.gov, and contribute to the conversation on Twitter and Facebook using hashtag #Pathtocures. Together, I know that we can provide hope to patients and families across our great country, and keep America at the forefront of innovation, and, by the way, create lots more jobs too.

Mr. Chairman, I yield back my balance of my time.

[The prepared statement of Mr. Upton follows:]

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Mr. {Pitts.} The chair thanks the gentleman.

Now recognize the Ranking Member of the Full Committee, Mr. Waxman, 5 minutes for an opening statement.

Mr. {Waxman.} Thank you, Mr. Chairman.

Today, we continue our work on the 21st Century Cures Initiative. These hearings are important. We need to ensure that patients gain access to new treatment and cures at the earliest possible time. At the same time, we need to recognize the strengths of our current system which has led to enormous breakthroughs in drugs and devices. FDA reviews and approves drugs faster than any other regulatory agency in the world. NIH and FDA are world leaders in clinical trial design, and in integrating the newest science into their policies and approaches, and our system protects the health of patients.

It is critical that we avoid any attempt to fix things that aren't broken, and, in the process, do harm to a system that is already working very well. We should create policies that foster scientific advances, but we should do so in a way that does not jeopardize public health.

Across the board, when we have an informal meeting, participants at the roundtable 2 weeks ago said that we need to assure that NIH has the resources necessary to maintain its national and international leadership in biomedical research, and I would welcome an opportunity to work with Chairman Upton, and all of our colleagues on both sides of the aisle, on accomplishing that goal.

The participants at that roundtable also indicated that FDA was generally excelling in drug and device oversight, and I was glad to hear that investment in the life sciences was booming. Mr. Left, one of the people there, attributed that success, at least in part, to some of the reforms we put into place in the 2012 FDA Safety and Innovation Act.

The PCAST report makes several recommendations relating to FDA. There are two I would particularly like to learn more about. One is the recommendation that FDA or Congress develop new voluntary pathway to facilitate the approval of drugs for special medical uses based on smaller clinical trials that would be needed for broader uses. A bipartisan Bill is introduced that would create such a pathway for antibiotics for serious or life-threatening infections for

which there are few, if any other, options. This is an area of increasingly dire need, and I think this Bill warrants serious consideration. As written, however, it does not achieve what PCAST described as an essential component of the pathway that the drug's labeling send a clear and effective signal that it should be reserved for use in the specific subgroup of patients for which it was approved. I would be interested in our witnesses telling us their views on this issue.

The other recommendation is the FDA undertake pilot projects to explore certain kinds of provisional approval pathways. These so-called adaptive approval pathways shift more of the data requirements to post-market studies, however, PCAST recommended that Congress not legislate in this area yet because serious questions still need to be addressed. These include appropriate evidentiary standards, protection of patients, and the ability to ensure that drugs are withdrawn if their effectiveness is not subsequently demonstrated. I would like to hear more about that.

I was disappointed that FDA and NIH were not invited to participate in today's hearing. I appreciate it, Mr.

Chairman, that you entered the FDA blog into the record. It shows the significant progress FDA has made in meeting the recommendations of the PCAST report.

And I would like to now yield the balance of my time to our colleague, Ms. DeGette, from the State of Colorado.

[The prepared statement of Mr. Waxman follows:]

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Ms. {DeGette.} Thank you very much, Mr. Waxman. And thanks, Mr. Chairman, for holding this hearing on the President's Council of Advisors on Science and Technology Report on Drug Innovation.

As has been mentioned, I joined with Chairman Upton to launch the 21st Century Cures Initiative about a month ago. We had a very successful kickoff roundtable with other members of this committee, where we heard from a number of experts, top leaders from the Administration, academia, research and industry, to dig deep into how we can effectively and efficiently tackle some of the more complex challenges in medicine.

As the next step in this endeavor, it was important to consider what types of recommendations relating to research and innovation have already been proposed. The report that we discuss today, as has been mentioned, provides 8 recommendations, ranging from federal funding for basic biomedical research, to improved drug evaluation. The report also highlighted what can happen when lawmakers work together on a bipartisan basis to pass legislation that addresses

emerging medical needs.

There are several Bills that I support, which have been mentioned both by the witnesses in their testimony, as well as the other Members today. A couple of them that have not been mentioned are the Antibiotic Development to Advance Patient Treatment, or ADAPT Act, and the Regenerative Medicine Promotion Act of 2014, of which I am the prime sponsor.

So there is a lot going on. I think the testimony today will be a good step along our path to figure out how we can work together towards research and innovation.

Thank you very much, Mr. Chairman.

[The prepared statement of Ms. DeGette follows:]

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Mr. {Pitts.} The chair thanks the gentlelady.

That concludes the opening statements, but opening statement of all the other Members will be made a part of the record.

We have one panel with us today, five witnesses, and I will introduce them in the order that they speak.

Dr. Garry Neil, Global Head of Research and Development for Medgenics; Ms. Sara Radcliffe, Executive Vice President, Biotechnology Industry Organiation; Mr. Frank Sasinowski, Director, Hyman, Phelps and McNamara; Mr. Jeff Allen, Executive Director, Friends of Cancer Research; Dr. Sean Tunis, Found and CEO, Center for Medical Technology Policy.

Thank you for coming. Your written testimony will be made a part of the record. You will be each given 5 minutes to summarize your testimony.

And, Dr. Neil, we will start with you. You are recognized for 5 minutes for your opening statement. Push the button, yeah.

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^STATEMENTS OF GARRY A. NEIL, M.D., GLOBAL HEAD OF RESEARCH AND DEVELOPMENT, MEDGENICS, INC.; SARA RADCLIFFE, EXECUTIVE VICE PRESIDENT OF HEALTH SECTION, BIOTECHNOLOGY INDUSTRY ORGANIZATION; FRANK J. SASINOWSKI, DIRECTOR, HYMAN, PHELPS AND MCNAMARA, P.C., ON BEHALF OF NATIONAL ORGANIZATION FOR RARE DISORDERS; JEFF ALLEN, EXECUTIVE DIRECTOR, FRIENDS OF CANCER RESEARCH; AND SEAN TUNIS, M.D., FOUNDER AND CHIEF EXECUTIVE OFFICER, CENTER FOR MEDICAL TECHNOLOGY POLICY (CMTP)

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^STATEMENT OF GARRY A. NEIL, M.D.

} Dr. {Neil.} Sorry. Chairman Pitts, Ranking Member Pallone, Ranking Member Waxman, and Members of the committee, thank you for the opportunity to testify before you this morning.

My name is Garry Neil and I head research and development in Medgenics, a small biotechnology company in Wayne, Pennsylvania, with operations in the U.S. and in Israel. My colleagues and I are working to bring novel ex

vivo gene therapies to patients with serious, rare and orphan diseases. I am a physician, and have spent the past 30 years in biomedical research and academia in industry, where I have worked in both large and small companies. I have also spent time in venture capital, and I have been engaged with a number of nonprofit organizations in support of the missions of FDA, NIH, and industrial research and development, and these include the Foundation for the NIH, the Reagan-Udall Foundation for the FDA, the Biomarkers Consortium, and TranCelerate Biomedical, an industry collaboration I helped found in 2012. I provided expert input into the 2012 PCAST report, and I am here today representing myself.

The American Biomedical Research and Development Ecosystem remains the envy of the world. Its value is immense, and I am sure that all of us in this room have benefitted from medical innovation driven by that system in some way or other. Biomedical innovation employs nearly 1 million people in the U.S., and exports from the biopharmaceutical industry reached nearly $47 billion in 2010, but beyond the economic impact, it provides increasingly effective treatments and hope for patients

everywhere.

The PCAST report identified a series of challenges and obstacles that continue to raise cost, lengthen timelines, and increase risk, including difficulties in translating basic scientific discoveries into therapies, inefficiency of clinical trials, and the need to streamline the regulatory process, as well as the need to ensure that appropriate incentives are in place to encourage investment in U.S. biomedical research. But since the release of that report, a number of important developments have occurred demonstrating the resilience of the system. The FDA Safety and Innovation Act of 2012 expanded the use of accelerated approval, and introduced a new breakthrough designation, both very helpful. TranCelerate Biomedical, as I mentioned, was launched as an industry collaboration to improve the efficiency of clinical trials. It currently has 16 member companies, and has embarked on a number of projects aimed at reducing operational bottlenecks faced by all sponsors. Early results are extremely encouraging. The accelerating medicines partnership, a public-private partnership between NIH, the pharmaceutical industry and patient advocacy groups, was

established and will address Alzheimer's Disease, diabetes and others.

At the Reagan-Udall Foundation, a public-private partnership created by Congress to support regulatory science, post-marketing safety surveillance is being advanced by the Innovation in Medical Evidence Development and Surveillance Project. And as Mr. Waxman noted, venture capital investment of biomedical research has started to increase again. Biotechnology investment dollars rose 8 percent in 2013 to $4.5 billion. These are encouraging signs, but much more needs to be done if we are going to reach the ambitious goals set in the PCAST report, and maintain our global leadership and life sciences, as well as address the healthcare challenges that confront the country now.

Additional help and leadership from Congress on this would be tremendously beneficial, and areas for Congress to target include facilitating the creation of clinical trial networks, investing in new biomarkers and clinical trial endpoints, increasing and sustaining funding for both FDA and NIH, expansion of public-private partnerships to support the

scientific missions of both FDA and NIH, providing FDA with increased flexibility to accelerate programs for lifesaving medicines, and examining existing incentives for capital investment of biomedical research.

Our company, like hundreds of other small innovative companies, faces many of these challenges every day. Our scientists, like virtually all industry scientists, are incredibly dedicated, driven and focused. Their ingenuity and problem-solving amazes me every day, and we are making rapid progress. We rely heavily upon collaboration with academic scientists who advise us, and also upon the regulators who help us to find the path forward. We also rely upon our investors. They risk their capital because they believe we will succeed. Clearly, there is no time or resource to spare. We lay every decision, every experiment with the utmost care. We understand the implications for our people, our investors, the country, but most importantly for the patients and their parents who are desperately waiting for cures.

I applaud the committee for undertaking this effort, and the sincere belief that it can result in positive change.

Enlightened, science-driven policy will allow companies like Medgenics to succeed, put the next generation of transformational therapies in the hands of caregivers around the world, and increase the competitiveness and prosperity of our country. Thank you.

[The prepared statement of Dr. Neil follows:]

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Mr. {Pitts.} The chair thanks the gentleman.

Now recognize Ms. Radcliffe 5 minutes for an opening statement.

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^STATEMENT OF SARA RADCLIFFE

} Ms. {Radcliffe.} Chairman Pitts, Ranking Member Pallone, and Members of the committee, my name is Sara Radcliffe, and I am the executive vice president for health of the Biotechnology Industry Organization, BIO. I thank you for the opportunity to testify here today.

BIO is the world's largest trade association, representing over 1,000 biotechnology companies, academic institutions, and state biotechnology centers across the United States. BIO applauds Chairman Upton, Representative Diana DeGette, and the committee members for undertaking the 21st Century Cures Initiative to examine what steps Congress can take to accelerate the pace of discovering and developing cures. We are excited to work with you to keep America the innovation capital of the world.

We also applaud the committee for holding a hearing on the PCAST report on drug innovation. It is critical that even in an environment of budgetary constraint, we do not yield to global competition and lose the next generation of

discoveries that could treat or cure the myriad of chronic and life-threatening diseases. From an emotional point of view, we have a duty to work to end the suffering these diseases cause. From an economic point of view, the U.S. can't afford to lose these advancements. Medicare spent over $100 billion in 2012 caring for individuals suffering from Alzheimer's Disease, and the expense is only going to increase. By 2030, almost one out of every five Americans, some 72 million people, will be 65 years or older. If we could delay the onset of Alzheimer's by just 5 years, we would save $50 billion per year. We have a national imperative to find new solutions, and this can only be accomplished if we all work together to create and defend policies that protect intellectual property, empower regulatory agencies to keep pace with science, encourage the development and adoption of modern approaches to drug development, promote a robust reimbursement environment, and continue to incentivize investment in scientific research.

The PCAST report noted that the overall efficiency of pharmaceutical R and D efforts has been declining steadily for more than 50 years. While there are many contributing

factors, it is widely recognized that increasing timelines and costs associated with clinical trials are key issues. More efficient clinical trials will reduce barriers to market for safe, innovative medicines.

In 2012, BIO launched our clinical modernization initiative to address four priority clinical research-related issues, some of which were also highlighted in the PCAST report. First, the use of centralized institutional review boards to promote greater efficiency, consistency and qualify of ethical oversight for multicenter clinical trials. Next, improving the FDA qualification process for drug development tools, including biomarkers. Additionally, advancing efforts by patient advocacy networks, medical centers, healthcare providers and other stakeholders to develop clinical trial networks and collaborative partnerships that could realize greater efficiency, consistency and quality in the conduct of clinical research. Finally, implementing a risk-based approach to clinical trial monitoring that leverages centralized data monitoring through electronic data capture systems can lead to significant efficiencies for clinical trial sponsors.

We would also like to applaud Congress for already having taken action of several of the PCAST recommendations with the passage of the Food and Drug Safety Innovation Act, FDASIA. For example, PCAST urged the FDA to expand the use of the accelerated approval pathway beyond the traditional areas of HIV, AIDS and oncology, and to be more open to the use of surrogate endpoints and intermediate clinical endpoints that are reasonably likely to predict clinical benefit, and that can be measured earlier in drug development, pending post-market confirmation. FDASIA encourages FDA to utilize the accelerated approval program more broadly, which may result in fewer, smaller or shorter clinical trials without compromising or altering the high standards of the FDA for the approval of drugs.

FDA's draft guidance on expedited programs will be very useful to sponsors, however, we encourage the Agency to further clarify the process for validating a novel endpoint, and for FDA to--and sponsors to discuss potential surrogate or clinical endpoints earlier in drug development. The PCAST report notes the drug developers have expressed frustration that it is difficult to get clear and timely answers

concerning the accessibility of specific predictors for accelerated approval. Without such clarity, the risk of employing such predictors during the lengthy drug development process is often too great to justify a significant investment.

Finally, there has been interest in an expedited approval process for medicines used for small populations. We look forward to continuing discussions with the committee on this issue.

Thank you for the opportunity to share with you our ideas.

[The prepared statement of Ms. Radcliffe follows:]

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Mr. {Pitts.} The chair thanks the gentlelady.

Now recognizes Mr. Sasinowski 5 minutes for his opening statement.

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^STATEMENT OF FRANK J. SASINOWSKI

} Mr. {Sasinowski.} Thank you for inviting me to testify.

I would like to introduce my colleagues, Alex Verone and James Valentine, who helped me prepare this testimony.

My testimony draws on 31 years of aiding new medicines get to patients in need. My career started at FDA in 1983, and I have a special passion for helping on therapies for rare diseases, because both my son and I have rare diseases. And I have been on the Board of Directors of NORD for the past 14 years. I am here today representing both myself and NORD. NORD, for over 40 years, has been the voice for the 30 million Americans with rare diseases.

I will be presenting 4 proposals for you to consider. My first proposal is for FDA to adopt a practice of considering the appropriateness of accelerated approval for each new therapy. Both PCAST and FDASIA exhort FDA to use its accelerated approval authority more. Last September, Alex Verone and I submitted to FDA our 65-page analysis of FDA's accelerated approvals. Our analysis shows that FDA

knows how to use this authority, and even how to use it flexibly, creatively and nimbly. In my view, what is needed now is simply to give this accelerated approval pathway greater visibility, so that it will be used more frequently for the benefit of patients, as was recommended by both PCAST and FDASIA.

So my first proposal is for this committee to encourage FDA to consider whether accelerated approval is appropriate for every new drug therapy that is brought by sponsors to the FDA.

My second proposal is for sponsors and FDA to use intermediate clinical endpoints, also known by its acronym of ICE, more often to secure accelerated approval. Alex and I analyzed the FDA accelerated approval precedents according to the 3 major factors that FDA described in the document that Ms. Radcliffe just mentioned, its June 2013 FDA guidance on expedited approvals. We analyzed the FDA approvals according to these three factors, and we found that two of these three factors are far less relevant to accelerated approvals, when accelerated approvals based on intermediate clinical endpoints or ICE, rather than surrogate endpoints.

Therefore, the quantity of evidence that sponsors must acquire and present to FDA, and that FDA then must review, may be substantially reduced if more accelerated approvals are based on intermediate clinical endpoints or ICE.

So to get more medicines to patients faster, this committee should encourage both sponsors and FDA simply to use more ICE.

My third proposal is to tap into the statutory authority for approving drugs that Congress created and gave to FDA in the 1997 FDAMA Law. This authority stated that FDA could approve a drug based on a single study with confirmatory evidence. Congress created this as an alternative to the standard Congress created in 1962, which has generally been interpreted to require two studies. This 1997 alternatives authority has been almost universally overlooked by all stakeholders, academia, sponsors, patients and even largely by the FDA as well.

I now ask my colleagues to hold up a chart. This chart is in my written testimony in greater detail, but this committee could propose that this simple chart be used at FDA Advisory Committee, and other FDA sponsor meetings and at

other forums to ensure that all the existing authorities are considered by every stakeholder for every new drug. Notice that the second line identifies that 1997 statutory authority or standard of a single study with confirmatory evidence, and the fourth line ensures that all recognize the potential of accelerated approval. So this one simple chart could help accomplish both of my first and third proposals.

Thank you, James and Alex.

My fourth proposal is for the committee to encourage FDA to issue guidance on cumulative distribution analyses of clinical study results. This could help understand the clinical meaningfulness of a new therapy. PCAST recommended that FDA issue more guidances to communicate innovative advances and regulatory science just like this one of cumulative distribution analyses.

So I am deeply honored by you to have been asked to appear before you today. Thank you.

[The prepared statement of Mr. Sasinowski follows:]

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Mr. {Pitts.} The chair thanks the gentleman.

Now recognize Mr. Allen 5 minutes for an opening statement.

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^STATEMENT OF JEFF ALLEN

} Mr. {Allen.} Good morning, Chairman Pitts, Ranking Member Pallone, and members of the subcommittee.

I am Jeff Allen, Executive Director of Friends of Cancer Research, a think-tank and advocacy organization dedicated to accelerating science and technology from bench to bedside.

It is an honor to be here, and I would also like to thank our founder and driving force, Ellen Sigal, who is here today as well.

Today, I would like to focus on a few of the key items identified within the report to the President, by describing areas in which there has been significant progress, and areas to which the committee might turn its attention and resources.

One key challenge that the working group explored was improving drug regulation at FDA. The authority and tools to fill FDA's monumental responsibility continues to evolve to keep pace with current science. I would like to provide a few examples that demonstrate this.

In collaboration with our expert colleagues from FDA, NIH, patient advocacy industry, and academia, we at Friends of Cancer Research proposed a series of approaches of how clinical testing could be modified to expedite the development of new targeted therapies that show dramatic clinical activity early in development. With the leadership of this committee, and your colleagues in the Senate, the creation of the new FDA program called the Breakthrough Therapies Designation was codified into law as part of the FDA Safety and Innovation Act.

FDA has been rapidly implementing the program in many serious disease settings, and, Mr. Chairman, I am happy to report that in just 2 years, 178 requests for breakthrough designation have been submitted, 44 have been granted, and 6 breakthrough therapies have been approved.

It has been estimated by some of the sponsors of the drugs that the breakthrough therapy program accelerated the development process by several years, without compromising the long-held standards for safety and efficacy. The all-hands-on-deck approach demonstrates the importance of the public-private collaboration that the designation brings to

enhanced science-based regulation, translating to reduced development times, increased investment in the biotech sector, and the improved health of patients that previously had few treatment options. This is an incredible example of Congress putting partisan politics aside, and acting deliberately to address one of our country's most pressing health issues.

Another key component of the report to the President explored ways of addressing inefficiencies in clinical trial conduct. There is no doubt that our antiquated patchwork clinical trial system makes developing new treatments a cumbersome, expensive and protracted process.

To being to address this issue directly, and truly change the course of how trials are done, Friends of Cancer Research is spearheading a project working with a large diverse set of partners from academia, industry, government and advocacy, to develop a modern-day clinical trial as innovative as the therapies it seeks to test. In this project, called Lung Map, a master protocol will govern how multiple drugs, each targeting a different biomarker, will be tested as a potential treatment for lung cancer. Each arm of

the study will test a different drug, and utilize cutting-edge screening technology to identify which patient is a molecular match to each arm. This will create a rapidly-evolving infrastructure that can simultaneously examine the safety and efficacy of multiple new drugs. Lung Map has the ability to reinvigorate the research enterprise, and rapidly facilitate the development of molecularly-targeted medicine. This approach has the ability to improve enrollment, enhance consistency, increase efficiency, reduce cost, and most importantly, improve patient lives.

One way that the FDA communicates to researchers and developers about new approaches or changes to current policy is through guidance documents, an interchange that is vital to modernizing the enterprise. The report recommends that external partnerships could be beneficial in providing input on scientific subjects that would be fit for guidance. Neutral public venues that can facilitate the exchange of ideas can greatly inform the topics and approaches that FDA may take when considering best practices and guidance development. Much like FDA benefits from hearing the challenges faced by the research community, the external

community gains from hearing from FDA. Processes and adequate funding levels need to be established to increase FDA's ability to gain external input and develop new guidance. This has the ability to greatly enhance the success of research endeavors, encourage innovation-- innovative collaborations, and can inform by the legislation.

In addition to the elements raised in the report, we at Friends of Cancer Research believe that consideration should also be given to opportunities in the development of companion diagnostics. Building on the foundation that FDA has provided through recent guidance, this committee could facilitate new policies to advance how novel technologies can inform the use of new drugs to ensure that the right patients have access to the right treatments at the right time.

The examples that I have provided today are case studies that can be learned from, and are steppingstones upon which more work can be done. Innovation is incremental, but with better understanding of the disease processes, these incremental steps toward improving health can and will be transformational. The regulatory framework has been put into place, and enhanced collaborations will be needed to uncover

new breakthroughs and alleviate inefficiencies. Aligning policies with the current state of science can enhance biomedical research and improve the lives of patients. The 21st Center Cures Initiative can be the next step toward that goal.

[The prepared statement of Mr. Allen follows:]

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Mr. {Pitts.} The Chair thanks the gentleman.

Now recognizes Dr. Tunis 5 minutes for an opening statement.

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^STATEMENT OF SEAN TUNIS, M.D.

} Dr. {Tunis.} Well, I would also like to thank Chairman Pitts, Mr. Pallone, and the members of the subcommittee for the chance to testify today.

Again, my name is Sean Tunis, and I am currently the CEO for the Center for Medical Technology Policy. It is a nonprofit that works on bringing together stakeholders to improve the quality and efficiency of clinical research.

I did serve as one of the invited experts to the PCAST council members and staff, and because of my former role as chief medical officer for the Medicare Program, I thought it would be most useful to reflect on these recommendations in the report from the perspective of the payer and the health system. It wasn't directly addressed in the report, but a number of the recommendations have implications for the health delivery system that I think need to be thought through more carefully in order to ensure that the recommendations can be implemented successful.

And I really think the--kind of the key message I wanted

to deliver and what it comes down to is that because many of the recommendations in the report essentially shift evidence requirements and data development from the pre-market space to the post-market space, in other words, the delivery system, it is going to be important to think about how it is going to be possible to efficiently conduct clinical research in the post-market environment, in other words, how do we embed the evidence development that is not generated preapproval in the context of delivering clinical care. And so I am going to offer 3 recommendations or suggestions about how that kind of evidence can be produced.

Just to briefly highlight the recommendations in the PCAST report that sort of have this effect, essentially, of shifting clinical research and evidence development to the post-market space, of course, there is the increased use of accelerated approval, depends more on intermediate and surrogate markers, and, therefore, the expectation is that more of the evidence of safety, effectiveness and even value are going to be generated while these products are in use in the delivery system. The special medical use as well as the adaptive licensing mechanisms also have the same effect,

which is, again, to require the ability to do efficient clinical research and data collection in the post-market space.

So in order for the PCAST recommendations, I think, to have the desired impact, which is to speed innovation, and to do that in a way that doesn't in some way compromise the expectation of safe, effective and high-value medications in clinical use, we are going to need, again, to think about how do we get that kind of data out of the delivery system.

As members of the subcommittee know very well, what is simultaneously going on to these innovation discussions is a lot of health systems reform that is increasingly pushing payers and the health systems to be looking for improved effectiveness, real-world effectiveness, and even the value of new medications. So at the same time as we are hoping to introduce new drugs into the healthcare system with less information about safety and efficacy, we are also putting pressure on payers and providers and health systems to demand more evidence of comparative effectiveness and value in order to be able to deliver high quality and efficient care. So we have got some tension between what we are trying to do on

each ends of this policy spectrum.

So, again, I think the solution to this is to think about ways in which we can be more efficient about data development in post-market studies. And basically, I will mention three kinds of components that I think are important to this. The first one is developing more clarity about what constitutes adequate evidence of effectiveness and value from the perspective of payers, clinicians and patients. And what I really mean by this is, in the same way that regulators produce guidance to explain what kinds of studies are necessary to achieve regulatory approval, there is currently nothing that provides guidance to product developers on what meets expectations of real-world effectiveness and value. And so, in a sense, the whole world of regulatory science, which is all about giving product developers clear guidance on clinical development, I think needs to be kind of mirrored in something you might call reimbursement science, which is how do you develop evidence for reimbursement decisions.

The second recommendation is, and some people might think reimbursement science is an oxymoron, but, you know, possibly we will make some progress.

The second and third recommendation, since I am running out of time, is--one is that we need to build infrastructure in the healthcare system to do better research. The NIH is working on that. And, finally, we are going to need to find reimbursement mechanisms that are actually conditional on collecting additional data. Medicare has used coverage with evidence development. There are other forms, but if we are actually going to be shifting these data collection requirements to post-approval, we need the payers to be willing to pay for things while they are being evaluated, much like the FDA has post-approval authority. I think the payers need to implement post-reimbursement authorities for--to collect the additional data on safety and effectiveness.

So thanks again for the opportunity to testify.

[The prepared statement of Dr. Tunis follows:]

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Mr. {Pitts.} The chair thanks the gentleman. Thanks all the witnesses for their prepared testimony. We will now begin questions and answers. I will begin the questioning and recognize myself 5 minutes for that purpose.

Dr. Neil, the PCAST report notes that the pharmaceutical industry is facing the largest patent cliff in its history. As a result, many companies are adopting more conservative approaches to research and development, particularly in areas with growing healthcare and economic burden, such as neurodegenerative diseases such as Alzheimer's and psychiatric diseases. What role could additional economic incentives play in driving R and D into these areas where there is a critical public health need, Dr. Neil?

Dr. {Neil.} I think they could be extremely valuable in helping to offset some of the cost associated with the risk, and the length of time these programs require. I do think though that it may be as productive or more productive to invest additional resources in things like endpoints, intermediate clinical endpoints, clinical endpoints. Often, we have found that as we try to study some of these

neurodegenerative diseases, they--it is a very long time between onset and ultimate disability, and if that is what needs to be used as an endpoint, it makes the feasibility of these trials much lower. So we haven't done enough to really invest, I think, in creating such endpoints, and I am thinking about Alzheimer's Disease, I am thinking about stroke as a couple of those, but there are many others, and some of the rarer neurodegenerative diseases have been inadequately studied with respect to their natural history as well. So I think some targeted efforts there would also be very helpful, as well as accelerating the pace of discovery work where diseases like schizophrenia, we have been out of really promising targets for some time.

Mr. {Pitts.} Okay. Ms. Radcliffe, what challenges do drug sponsors and the FDA face today in the use of surrogate endpoints and biomarkers, and what are the current barriers to their more widespread adoption and use? And maybe you want to, just for the general public, tell us what biomarkers, endpoints, define them for us too briefly.

Ms. {Radcliffe.} Sure. Absolutely. So biomarkers, and the terms biomarkers and endpoints are used in various

different ways in the scientific community, so I am going to tell you the way in which I urge that we understand those terms. A biomarker is really a signal of--it is a biological signal of another biological process. It is really that simple. A biomarker can be used in many different ways in research and development. For it to be used in the regulatory context, all parties have to have a great confidence in the relationship between the biological signal and the biological process that it is signaling. An endpoint in regulatory terms, a clinical endpoint, is something that affects how a patient feels, functions or survives. So in relatively simple terms, it is something that the patient will actually recognize. A surrogate endpoint is a marker that can point toward the ultimate clinical benefit for a patient. So an example of that would be viral load is a surrogate endpoint for a treatment effect for HIV and AIDS drugs. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier on in the disease process. And so an example of an intermediate clinical endpoint would be something that is called forced vital capacity, that is the ability for a patient to expel a large

amount of air, and it can be a good marker of progression and possibly treatment effect in neurodegenerative disorders. And so the use of intermediate clinical endpoints can expedite drug development because you are now working toward treatment of an endpoint that you are seeing earlier on in the disease process, and that may enable you to ward off further--effects further down the line in the disease process. So why is it important for our companies? The use of surrogate endpoints and intermediate clinical endpoints can expedite drug development, and enable us to get a product to patients earlier with smaller and shorter clinical trials. In terms of the obstacles that we face, as I said, there is not the kind of clarity that we would like around what FDA will accept as a surrogate endpoint, and what FDA will accept as an intermediate clinical endpoint. The evidentiary standards that FDA is likely to require at this time really require a lot more discussion with the Agency, and also just in terms of process, as I said in my testimony, there isn't at this time a good practice of companies and sponsors talking about intermediate clinical endpoints earlier on in the drug development process, so that you can really work

toward the use of those endpoints as you develop your submission to the FDA.

Mr. {Pitts.} The chair thanks the gentlelady.

My time has expired. Recognize the ranking member 5 minutes for questions.

Mr. {Pallone.} Thank you, Mr. Chairman.

I wanted to explore in some detail one of the recommendations from the PCAST report, specifically, recommendation number three, which states that FDA should expand the use of its existing authorities for accelerated approval, and for confirmatory evidence. And as I understand it, there are already a few pathways in the current law and regulations for the expedited review of drugs, including fast track, breakthrough therapy, accelerated approval and priority review, and the goal of all these pathways is to speed the development and availability of new treatments to patients at the earliest possible time. Just a couple of years ago in the 2012 FDA Safety Innovation Act, we updated the fast track approval mechanism and established the breakthrough therapy path. And then, of course, the 21st Century Cures Initiative seems to have been promoted at least

in part by what has been described as a regulatory system that is a relic of the past, but this is confusing to me because we just finished updating the system, and providing FDA with new tools. So I also didn't hear anyone at this-- the first roundtable with the 21st Century Cures Initiative who would describe FDA's drug regulatory program as somehow out-of-date.

So I would like to hear more from our experts here today on how effectively FDA has been using these current authorities, and where there might be room for improvement.

First, let me ask Dr. Allen. Your testimony describes FDA's use of the breakthrough therapy pathway, which sounds like it has been a real success. Can you say a little more about that, and describe how FDA has used any of the other expedited review authorities with respect to cancer drugs, and have you identified any problems or issues in its application of these authorities?

Mr. {Allen.} Sure. Well, I again want to thank the committee for their leadership in creating such a designation.

The tools that FDA currently has, based on the 2012 law

and others, have been widely used in cancer. I think well over a third of all anticancer drugs have utilized the accelerated approval process, for example. So it certainly is valuable. The purpose of the breakthrough therapy designation was to, as you say, Mr. Pallone, too, advance and give the flexibility for FDA to respond to the current state of science, because what we are seeing in oncology and many other genetically-driven diseases is the ability to target different genetic alterations, and stop the progression of the disease. And this calls for a different way of doing business, and we believe that is what the FDA is doing, and they have robustly implemented the new breakthrough therapies provision and are excising it regularly.

I think it is worth noting the resource intensity of this program. It certainly is serving its purpose of getting the most promising therapies to patients, but the resources required to do so are not insignificant, and I know there is a hearing elsewhere today considering the funding for FDA, and I would encourage them to do what they can to support that.

I think the historic basis of speaking to those

regulations is because there were laws in 1960 that established the safety and efficacy standard, and those are extremely important that we continue to optimize regulation and drug development within those important standards.

Mr. {Pallone.} All right, thanks.

Mr. Sasinowski, your testimony also describes the ways in which FDA has used these authorities over the years, and it sounds like you would also say that FDA uses them frequently and prudently. Is that correct?

Mr. {Sasinowski.} Mr. Pallone, prudently but not frequently. The analysis that my colleague, Alex Verone, and I did, we looked at all of the FDA accelerated approvals for therapies other than cancer, and Mr. Allen is right, it is often used in cancer. I was at FDA during the AIDS crisis, and so I was part of the group that helped create Subpart H, which was very useful for stemming the AIDS crisis. So accelerated approval has been used, but you will notice in our PCAST report that you cite, Mr. Pallone, that 87--we say in the PCAST report 87 percent of all the accelerated approvals have been for cancer and for AIDS. And so what Mr. Verone and I did is we looked at every accelerated approval

from the mid-'80s through June 2013. We found only 19 drugs that had been approved, not for cancer, not for AIDS, under accelerated approval. We found that the FDA did use accelerated approval appropriately in those 19 cases, but it was only 19 cases, Mr. Pallone, and that is why I think PCAST said we should use it more. I think that is why this committee and Congress said in FDASIA, FDA, use it more. That is why there are 2 women who I was surprised to see here, who are in this room, who have between the 2 of them, 3 boys with DMD; Christine McSherry and Jane McNeary, and I know that they represent, as a member of NORD, they represent the kind of Americans who are suffering and who are looking for FDA to use accelerated approval more often for conditions that are not AIDS, not cancer.

So I think appropriately they used it, and that is why I suggest this chart, because I have been to thousands of FDA meetings since I left the FDA, with sponsors seldom does the word Subpart H, accelerated approval or fast track ever get mentioned. People are not focused on it, that is why I urge you to consider exhorting the FDA through some simple mechanisms like a chart, like at every advisory committee

when the chair of an advisory committee turns to the FDA and say, what are we supposed to do with this date. We know what the Congress' standard was in 1962, two adequate and well-controlled studies. This is a rare disease. Something like Duchenne Muscular Dystrophy. We don't have two adequate and well-controlled studies, so what are we supposed to do?

Well, there is a lot of hemming and hawing, and I think that if we had a chart like this that was proposed, that would summarize in a clear way that there are alternate authorities like the 1997 authority that Congress created, which was the single study with confirmatory evidence, and I have explained that in great detail in my written testimony, that that would be very useful, as well as to remind everybody of accelerated approval.

Mr. Pallone, I was at a hearing just last summer, in August 2013, for a drug for autosomal dominant polycystic kidney disease. My spiritual director had his nephew die of this disease. I know people who have died of this rare disease. It is a terrible disease, and yet not once did anyone ever mention at that hearing the possibility of accelerated approval, even though it is a serious disease, it

is for a situation where there are no approved therapies, it is ripe for consideration under accelerated approval, just like PCAST, just like you and FDASIA said FDA should do, and yet it was never considered.

So I am struggling to think of ways, Mr. Pallone and the committee, to try to bring this forward in practical ways, and that is why I come up with something as simple as a chart. It might seem pedantic, it might seem trite, but I think sometimes simple things work. And so I think you are right when my analysis shows that the FDA has used this authority appropriately and prudently, but not frequently. And the other thing that has been completely overlooked is that single study with confirmatory evidence standard, which Congress created in 1997 and FDA seldom used.

Mr. {Pallone.} Thank you.

Mr. {Pitts.} The chair thanks the gentleman.

Now recognize the Vice Chair of the Subcommittee, Dr. Burgess, 5 minutes for questions.

Dr. {Burgess.} Thank you, Mr. Chairman. And I actually appreciate that last part of your discussion, Mr. Sasinowski. You started at the FDA just a couple of years after I started

in private practice, and I can recall back in the '80s being frustrated by the fact that it seemed like there were new therapies that were available in Europe, and it took us forever to get them in this country. Of course, Chairman Waxman, or Ranking Member Waxman, deserves a lot of credit for starting the user fee agreements, which we reauthorized in the last Congress.

Dr. Neil, I wanted to ask you just very quickly if you could--you mentioned that your company was involved in novel ex vivo gene therapies. Could you give us a synopsis or a summary of--without violating, obviously, propriety interests, but can you tell us some of the directions that you are--in which you are working?

Dr. {Neil.} Yes. The core of our technology is something called the bio pump. So we remove a small piece of dermis, the layer just below the skin, about half the size of a toothpick, and we transduce that with a viral vector to express a transgene, a protein that a patient with a rare and orphan disease might not express at all, or might express in too low a quantity, and it is causing their disease, and they could benefit from having this restored. And after the

transduction, all of the viral antigens are washed away and we re-implant this small piece of tissue back into the patient, so the patient effectively manufactures their own protein that they could not manufacture before, or in a sufficient quantity, and that then addresses, we hope, the disease in question.

And we are aiming this technology at a number of rare and orphan diseases that could benefit.

Dr. {Burgess.} And in addition to rare diseases, are there more common diseases that you are also working toward?

Dr. {Neil.} Yes, that is very likely, but I think that we shouldn't overlook the fact that very often we can learn so much by studying a rare and orphan disease initially because the population is enriched, we understand the mechanisms much better, and then we can apply the lessons that we have learned to the larger syndromic diseases.

Dr. {Burgess.} Since a lot of this panel, or a this hearing today, deals with the regulatory aspects, how is that--how has your experience been then when you take this information back to the FDA for regulatory approval? Do they understand what you are doing, are they able to give you the

proper direction about how to structure your studies so that regulatory approval can be achieved?

Dr. {Neil.} Yes, our interactions with FDA have been a little bit earlier than approval, because we are just embarking on some of these programs in the clinic, but those interactions have been very positive, and they seem very helpful and very interested in the technology, but we and other companies are now bringing to FDA very novel therapies which incorporate many different elements, such as medical devices, gene therapy, tissue transplant and so on, and I think that, and I directed some of my testimony toward that, the increasing complexity of these types of treatments, something that FDA is going to need to invest in expertise in--

Dr. {Burgess.} That is--

Dr. {Neil.} --culture.

Dr. {Burgess.} That is correct. I don't mean to interrupt you because I am going to run out of time, but that is correct, they don't have the--

Dr. {Neil.} Right.

Dr. {Burgess.} --expertise currently. They do have to

develop it.

Dr. Tunis, I really appreciated your end of the discussion. You talked about from the payer aspect to the CMS aspect. Certainly we want to avoid the public relations disasters that were of Asten and Provenge from a year or two ago, and one of my concerns through a lot of the hearings that we have had here is anyone looking at the end use of this, I mean, okay, we have got NIH developing, we have got the FDA which is going to regulate and/or approve, but we also need to involve the payer at some point to let them know what is coming so that they can appropriately adjust. So I do appreciate you bringing that up, and I think oftentimes we overlook that aspect of the regulatory pathway.

Dr. {Neil.} Yeah, and, you know, I think, just to point out, I think, you know, the payers are often viewed collectively as, you know, not in favor of innovation or somehow resistant to, you know, new technologies, and while, you know, there are certain ways in which that is true, I think it is also true that the health system understands that innovation is potentially a way to get better outcomes at even lost costs, you know. Treating disease is obviously,

you know, cheaper than treating a--you know, treating it forever is cheaper than having to continue to treat it in an ongoing way.

So the challenge really is that--and as I said, I do think the payers get left out of these conversations. There were a couple of payers on the PCAST committee, and again, most of the discussion about the--is about regulatory issues, but, you know, a metaphor I use is you don't want to create this superhighway of innovation in the regulatory space, and then have a gravel road, you know--

Dr. {Burgess.} Um-hum.

Dr. {Neil.} --in the reimbursement space for those--

Dr. {Burgess.} And I have been down that gravel road. You know, when I was in medical school, we learned about the treatment of peptic ulcer disease. It was a surgery, a highly selective vagotomy of removal of part of your body, but I also remember going to a luncheon meeting back in the '70's where Dr. Fordtran from Dallas came down and talked about this new idea he had of a histamine blocker to deal with ulcer disease. And, of course, now half the country is on proton pump inhibitors, and the highly selective vagotomy

is in the Smithsonian Institution. No one does them anymore. You would have to go--it itself is a rare disease because you--no one has to have that anymore. It is hard to get the same, you know, to be able to account for the savings that Dr. Fordtran created with the development of his product, because all of the baby boomers who at that point were in medical school, but were on their way to developing ulcer disease, would have required that surgery at some point in their future.

Dr. {Neil.} To say nothing of them cured of antibiotic therapy for helicobacter pylori, which--

Dr. {Burgess.} Sure.

Dr. {Neil.} Yeah.

Dr. {Burgess.} Thank you, Mr. Chairman. He--his gavel is the surrogate endpoint for my questioning.

Mr. {Pitts.} We will have a second round.

The chair thanks the gentleman. Now recognize the gentleman from Texas, Mr. Green, 5 minutes for questions.

Mr. {Green.} Thank you, Mr. Chairman. And, again, thank our witnesses for your testimony today.

Without greater investment in antibiotics, we will face

a future that resembles the days before these miracle drugs were developed, one in which people died of common infections, and many medical advances that we take for granted today would become impossible, including surgery, chemotherapy and organ transplantation.

Dr. Neil, you mentioned in your statement, in 2012, PCAST recommended a limited population drug approval pathway in order to facilitate drug development. PCAST specifically identified antibiotics as an area where this pathway could-- would be important, and as we know, the need for new antibiotics is urgent. The World Health Organization reiterated just this month on a report of antibiotic resistance which said it is a very real potential for post-antibiotic here in the near future.

My colleague, Dr. Gingrey, and I introduced the Adapt Act which would create the pathway PCAST described. FDA officials from the Commissioner down have talked about the Agency's desire to work with Congress to get this done. We are eager for Congress to quick--act quickly and given the urgency of the situation.

Dr. Neil, could you explain how this pathway would

benefit antibiotic development?

Dr. {Neil.} I think that--yeah, it is on. I think it would benefit it tremendously, not only the development of it, but also the appropriate use of these new drugs once they get into clinical use. But the idea that one can identify very easily through surrogate markers the appropriate population with a serious infection, and be able to address that much more quickly, speed these antibiotics to the market, I think is a terrific one. And not only that, I think what we learn from this and how to implement it can be applied to other serious diseases later on, potentially.

Mr. {Green.} Okay. Dr. Allen, cancer patients are particularly at risk for serious bacterial infections. Patients undergoing chemotherapy are--have suppressed immune systems, making it more difficult for them to fight off other diseases. Without antibiotics, chemotherapy would be significantly more dangerous.

Dr. Allen, you talk about a limited population pathway for antibiotics. Could--this could be important to cancer patients. Can you talk to us about that?

Mr. {Allen.} Sure. Well, as you mentioned, and thank

you for your leadership in this area, risk of infection for cancer patients is certainly increased, and it has the potential to interrupt their treatment on a chemotherapy or other anticancer drug, that they may have to stop that treatment, and it could have a detrimental effect toward harnessing the growth of the cancer. Even more detrimentally is if a cancer patient who is immune-compromised is infected with microbial infection, it poses them at risk for serious adverse events and fatality. So it is not insignificant here both in the treatment of the cancer, but also in the survival of the patient.

Mr. {Green.} Okay. In 1990, there were almost 20 pharmaceutical companies with large antibiotic research and development programs. Today, there are only two or three large companies with strong active programs, and only a small number of companies have more limited programs.

Ms. Radcliffe, in your testimony, you mentioned that the Adapt Act and the importance of the voluntary pathway can help foster novel drug development. Can you elaborate on how this kind of pathway would address some of the economic challenges, particularly the size, the cost and time it takes

to complete clinical trials that may be hindering antibiotic--investment in antibiotics?

Ms. {Radcliffe.} Yes, certainly. BIO supports the Adapt Act, and we thank you very much as well as Representative Gingrey for your work on developing this pathway. It has to walk a very fine line.

Mr. {Green.} Yeah.

Ms. {Radcliffe.} It is important that sponsors be able to seek the designation early, or follow the pathway early on in development so that they can gain the benefits of being able to design a clinical pathway in a smaller population, and with attention from FDA as to the greatest clinical efficiency in those trials. This Bill would permit that to happen. It is also important that the pathway not infringe on the pathway--on the practice of medicine, and that is an important protection for patients. Physicians have to be able to use a product that they believe to be the best for their patient and the circumstances where the patient finds him or herself. And so, therefore, it is very important that such a pathway not infringe on the path--on the practice of medicine, and the Bill that you have introduced does that.

So we think that it will be a very great--of very great assistance to sponsors in terms of incentivizing work in this incredibly important area for antibiotic resistance.

Mr. {Green.} Thank you, Mr. Chairman. I know I am out of time. To meet this crisis, we need a multi-prong approach that includes enhanced monitoring, better use of antibiotics, and investment in new therapies, and we can no longer ignore the risk of antibiotic resistance, the epidemic and the growing number of lives these superbugs claim.

And I thank you for having the hearing today.

Mr. {Pitts.} The chair thanks the gentleman.

Now recognize the gentleman from Illinois, Mr. Shimkus, 5 minutes for questions.

Mr. {Shimkus.} Thank you, Mr. Chairman. It is great to have you all here.

I have been interested, there is a Washington Post story published May 16 on the movement by states on right-to-try laws. The one column--part of the end of the article, and, Mr. Chairman, if we could submit it for the record. I--

Mr. {Pitts.} Without objection, so ordered.

[The information follows:]

This is a preliminary, unedited transcript. The statements within may be inaccurate, incomplete, or misattributed to the speaker. A link to the final, official transcript will be posted on the Committee's website as soon as it is available.

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Mr. {Shimkus.} There is a story about the spouse, Amy Auden, from Lone Tree, Colorado, who had--her husband had melanoma, 2-year battle, the last year they tried to get a promising drug, couldn't get it, and he has since passed. And her comment is, of course there was a chance Nick would have been in the 52 percent of the people who are responding to the drug, however, a 52 percent chance of life is better than a 0 percent chance of life, which was the dilemma that this family was placed in. And, hence, you see states moving to address this. It is not--what--a brief comment on this movement by states on--to right-to-try laws, and that is probably symptomatic of a slow process of getting drug therapies quickly to the market. Is that true? Let us just go from left to right, if you want? And if you don't want to answer, that is fine. I mean it is--

Dr. {Neil.} Well, in my experience, FDA has always been very compliant in getting patients, you know, into small trials or compassionate use trials. To me, the issue has always been for smaller companies, having the resources to be able to provide that, and I think mechanisms--

Mr. {Shimkus.} This wasn't a small company that she had to deal with--

Dr. {Neil.} Yeah.

Mr. {Shimkus.} --so--

Dr. {Neil.} Well, yeah, I think that there should be some way for companies to recover their cost, and to get patients into trials, and to be able to collect the information that you need to make that--

Mr. {Shimkus.} Right.

Dr. {Neil.} --usable.

Mr. {Shimkus.} And please kind of go quickly. I have got--actually my two official questions that I need to get to.

Ms. {Radcliffe.} So this is a very, very difficult issue. BIO has a board-level BIO Ethics Committee which is currently involved in taking a deep look at the issues around expanded access. I think everyone understands that if somebody in their own family were in such a situation that they needed an investigational product, I think most of us would do everything that we could to--

Ms. {Shimkus.} But is the statement--

Ms. {Radcliffe.} --ensure--

Mr. {Shimkus.} --about the process--

Ms. {Radcliffe.} Yeah.

Mr. {Shimkus.} --and how slow and methodical, and people who--it is happening, I mean these are--there are three states I think, there is Colorado, one is going to be signed into law on Saturday, from what I am reading, and that is a response to people feel that they are not getting a chance to fight for their life, and they are being held up either in the--let me move forward. I--because I need to move on on these two other questions. On the presence counsel raises the fact that in recent years there has been a regulatory uncertainty about a variety of important issues that has hindered investment and innovation. One such issue is combination of therapies and studies that are required for their approval.

Has FDA since provided sufficient clarity in this area, or is there need to ensure greater regulatory certainty for companies to spur further innovation in this increasingly important area of drug development? Anyone want to try it?

Dr. {Neil.} I think there is further need, particularly

outside of cancer, to echo Mr. Sasinowski's comments earlier.

Mr. {Shimkus.} Great, thank you. Anyone else?

Dr. {Tunis.} Yeah, you know, and I would just add again, sort of related to some of the comments I made in my testimony, that the better equipped, you know, we are in the context of delivering healthcare to get the additional information about, you know, products that are approved through an accelerated pathway, I think the more the FDA can count on some of the unanswered questions about safety, you know, safety and effectiveness to be efficient--to be answered at least at some point, and then the opportunity to accelerate--to use the accelerated authorities more frequently, I think, is enhanced as the delivery system gets better at filling in what is not studied pre-market.

Mr. {Shimkus.} Let me finish with this last question, and the rest I will submit for the record.

A second distinct area that report highlights which is of particular interest to me is the issue surrounding the certainty and the regulatory pathway when it comes to therapies for which patients are picked based upon companion diagnostics. The companion diagnostic may or may not be

approved already, adding an additional layer of complexity for the sponsor.

Do any of you witnesses have experience in this area to comment on what needs to be done to encourage investment and innovation for these personalized approaches?

Mr. {Allen.} So the trial that I mentioned with regards to lung cancer is working to try and advance these technologies through the regulatory process, by using new technologies that have the ability within a single test to monitor the activity and presence of different genetic alterations. So it has the ability to really reform the current single test paradigm with a single drug. But I think the FDA has been proactive in issuing guidance documents both from the drug and diagnostic side, to begin to lay out what their feelings are on how to generate this evidence, but some of this is also an artifact of making sure that there is a robust research enterprise to really understand which are those true alterations that are driving different diseases.

Mr. {Shimkus.} Great, thank you.

My time has expired. Thank you, Mr. Chairman.

Mr. {Pitts.} The chair thanks the gentleman.

Now recognize the Ranking Member of the Full Committee, Mr. Waxman, 5 minutes for questions.

Mr. {Waxman.} Thank you, Mr. Chairman.

The PCAST report's fourth recommendation is the creation of a new pathway that manufacturers could choose to use for initial approval of drugs shown to be safe and effective in a specific subgroup of patients. The report notes that such approvals could sometimes be based on relatively small and rapid clinical trials showing a favorable safety and effectiveness risk benefit ratio for the narrow population most in need of the drug, however, it notes that for such a pathway to work, FDA would have to be confident that the drug generally would not be used beyond the limited population for which it was evaluated and intended.

Dr. Allen, do you think the pathway makes sense if FDA does not have adequate authority to ensure that the designation is used to inform potential users and payers of the special standing and circumstances surrounding approval of the drug?

Mr. {Allen.} I think it is important to state that the intention of the limited population pathway is to still

operate within the confines of safety and efficacy, and that is not altered. I think that ensuring appropriate use of these types of products will require a great deal of interaction with the medical community, and make sure--in making sure that the appropriate lines of communications are present, to make sure that the benefit risk profile within that subset is maintained, and communicating clearly that the benefit risk for the entirety of the population may not be known yet, but those patients with the most life-threatening version of that disease don't have the time to wait. So this allows for access for those with the most severe form of a relatively common illness.

Mr. {Waxman.} So you think that if a--if they have adequate authority to designate this information, that that would be important if they are going to release this drug before it is approved for the general population?

Mr. {Allen.} Yes, certainly, and having the ability to communicate is largely based on the label, as it is with all prescription drugs--

Mr. {Waxman.} Um-hum.

Mr. {Allen.} --but in this case, it would be important

to indicate if there is--if this has only been tested in the most severely ill patients, through use of some sort of symbol--

Mr. {Waxman.} Um-hum.

Mr. {Allen.} --or logo to communicate it, but also the ability to pre-review marketing material, and that has been an effective strategy in other areas such as accelerated approval.

Mr. {Waxman.} Let me turn to another recommendation in the report. Recommendation five has to do with another new potential mechanism for more quickly making new therapies available to patients, a so-called adaptive approval. As I understand it, adaptive approval refers to the concept that there would be a series of approval stages that would gradually allow a new therapy to be marketed for broader patient population, so as more is learned about a drug, the use of it could be expanded.

The PCAST apparently explored this concept extensively, however, in its final recommendation, it said that Congress should not legislate this new pathway, instead, any use of this approach should instead be tested in pilot projects.

Dr. Allen, can you say more about why PCAST was hesitant to have any legislation on this pathway at this point?

Mr. {Allen.} Well, I don't want to speak on behalf of the entire work group, but, you know, from my perspective, it is very difficult to have one set of rules that governs a very diverse set of products--

Mr. {Waxman.} Um-hum.

Mr. {Allen.} --and given the pace at which science is accelerating, I think many of the other witnesses on the panel today have talked about some really innovative approaches to different diseases, and it is hard to really kind of draw a single line in the sand. A drug for prevention is very different than a drug for late-stage pancreatic cancer, and the benefit risk profile of that is very different--

Mr. {Waxman.} Um-hum.

Mr. {Allen.} --and so it is hard to codify that into law.

Mr. {Waxman.} Mr. Sasinowski, do you have anything to add on this? Why did PCAST recommend against legislation?

Mr. {Sasinowski.} I cannot speak for PCAST, just as Mr.

Allen can't, but for my own perspective, and that from NORD, is our perspective is that it was premature. It merits exploration, but at this time, you know, trying to integrate that and come up with a system, we didn't have a program in front of us that had enough granularity for us to speak to it with any confidence. So I think that this is in the exploratory world.

Mr. {Waxman.} And I appreciate that.

Let me, Mr. Chairman, just briefly mention one other critical issue that deserves a hearing in and of itself. We need new therapies to be marketed but we have got to address high prices for these therapies. There are no good--there are no--they are no good for anyone if we can't afford them. And I have a recent article from the New York Times that describes the hardships faced by patients with chronic diseases who can't afford the price of their treatments. It notes that the high prices of treatments for diabetes and other chronic diseases are a major contributor to the U.S., $2.7 trillion annual health bill. This is an issue we will have to address at some point. And I would ask unanimous consent this article be made part of the record.

Mr. {Pitts.} Without objection, so ordered.

[The information follows:]

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

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Mr. {Waxman.} Thank you.

Mr. {Pitts.} The chair thanks the gentleman.

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

Mr. {Lance.} Thank you, Mr. Chairman. And good morning to you all.

The state I represent, New Jersey, represented as well by Ranking Member Pallone, is certainly among the medicine chests of the world, and a center of significant biomedical innovation. We are the proud home to tens of thousands of jobs in these life-saving industries. These companies reinvest hundreds of millions of dollars each year back into R and D in order to bring much-needed therapies to patients, to market.

I am deeply concerned about the slashing of R and D budgets that may look good on a financial spreadsheet, but I think would be tragic for patients moving forward. I ask this out of a concern regarding recent news on certain potential acquiring companies' intentions to slash R and D spending, for example, in the case of Allergan, a company

that provides hundreds of jobs in the congressional district I serve. A potential buyer of Allergan has stated that it can achieve cost synergies by cutting approximately $1 billion in investment in R and D, and eliminate 5,000 high-quality U.S. jobs, as well as lower its tax rate from 26 percent to low single digits. Companies like Allergan invest significant capital in R and D in order to continue to development treatments for unmet medical needs. These investments not only support high-skilled, well-paying jobs, but also continue to deliver new, potentially life-saving products in the development pipeline. I am concerned that this could become the model for other such mergers, and we would lose the engine for innovation and growth here in the United States.

To you, Ms. Radcliffe, how dependent are future cures on robust commitments in the private sector to research and development?

Ms. {Radcliffe.} Thank you. So BIO is unable to comment on any particular companies--

Mr. {Lance.} Yes, I realize that but--

Ms. {Radcliffe.} --businesses and things--

Mr. {Lance.} --in general, please.

Ms. {Radcliffe.} We are not familiar with that. I personally am not familiar with the situation, specifically in the case that you mentioned, to make any comment whatsoever. Obviously, the mission of BIO is to ensure that there is a research--a robust research and development pipeline in the United States for the development of new cures that will help patients and meet unmet medical needs.

Mr. {Lance.} And do you believe that the level of research and development now in this country, in private companies, that, in general, that is the level that should continue and perhaps even increase?

Ms. {Radcliffe.} Again, not commenting on any specific company, because there--every individual company may have its own situation with respect to exactly the level of research and development that it is conducting, as opposed to research and development that it licenses in or that are conducted in partnerships and so forth, however, I think that it--for BIO, again, the level of research and development in the United States is extremely important, as I said in my testimony, it is very important that we as a nation continue to elevate our

research and development for the purposes of meeting unmet medical needs for patients, and also in terms of global competitiveness.

Mr. {Lance.} So in general, you favor more research development funding as opposed to fewer funds in that portion of the larger whole?

Ms. {Radcliffe.} As a general principle, yes.

Mr. {Lance.} Yes.

Ms. {Radcliffe.} And, of course, it would matter as to how that research and development funding were specifically spent.

Mr. {Lance.} Thank you.

To the panel in general, the President's Council of Advisors on Science and Technology states that one of the most powerful incentives for drug development is granting periods of exclusivity to new drugs. It also mentions the economic disincentives created by long clinical trials required for conditions such as Alzheimer's Disease. The President's council acknowledges that engaging in the economic analyses required to provide potential policy changes is beyond the scope of the report and outside core

experience. That being said, Hatch-Waxman was enacted in 1984, and it is indisputable that the time and cost it takes to develop a drug has significantly increased over the course of the last 3 decades. There are many potential therapies that would address other unmet medical needs, such as rare diseases and mental health, areas in which I am involved; I am the Republican chair of the Rare Disease Caucus, that lack sufficient patent protection.

To the panel in general, what are your thoughts on using data exclusivity to address these issues?

Mr. {Sasinowski.} You know, first, on behalf of NORD, I want to acknowledge the--Congressman Lance's leadership in the congressional caucus on rare diseases.

Mr. {Lance.} Thank you very much.

Mr. {Sasinowski.} We have so awarded you, you know, on behalf of your leadership in that area, and we believe that the ability of all--let us say the Orphan Drug Exclusivity Act had a tremendous incentive that has sparked a great deal of research and development for rare diseases. You heard even Dr. Neil mention that his company is moving in the area of rare diseases, maybe in part because of the economic

incentive that is provided by the Orphan Drug Act. So these kind of incentives have been powerful. Every person or every organization that has examined it has found their utility. The question though that is sometimes raised, Congressman Lance, is should we, for instance, expand the exclusivity, should we enter into the orphan drug exclusivity now that we have other forms of protections that exceed 7 years, perhaps in order to re-establish the primacy of orphan drug exclusivity that should be extended beyond 7 years. So these questions have been raised, and they are serious questions that I think that merit further discussion.

Mr. {Lance.} Thank you.

I yield back the balance of my time.

Mr. {Pitts.} The chair thanks the gentleman.

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

Mr. {Griffith.} Mr. Allen, you indicated it is hard to legislate or to come up with a good legislative model when you have all these different diseases, and you have some which are fatal and quickly fatal, others which are chronic. Don't you think simpler might be better, and that maybe Mr.

Sasinowski's chart might be of some help in that regard?

Mr. {Allen.} Absolutely, and I think that was what was intended and what the committee enacted through the breakthrough therapies designation; a very simple requirement of early clinical activities showing a substantial improvement that results in a very flexible, intensive collaboration to get that drug through the process.

Mr. {Griffith.} And sometimes we get fancy. We like to do things that are more complicated.

Mr. Sasinowski, you want to talk about your chart again for a minute? Somebody might not have been watching earlier.

Mr. {Sasinowski.} Well, thank you, Congressman Griffith. As a fellow Virginian, I appreciate that.

I am holding up a paperclip. Sometimes a paperclip can do an awful lot of good. And so I have been involved in this area of drug innovation, like I said, for more than 3 decades, and I have wrestled with this question of what can we do as--to achieve what we all want to achieve, like to accelerate approvals. And when I have been involved in this process, I see how often, shockingly, these very simple concepts that the Congress has created, such as fast track,

you know, are not considered, and if we just give them more visibility, it sounds so simple, but if we required that at every new therapy that were to come before the FDA, there would be a simple question put, is this therapy one that would be a candidate for accelerated approval, it wouldn't take hardly any resources to consider that, it wouldn't delay at all the review of it, but it might spark the very kind of thing that others around the table here have talked to, that if we are going to engage in accelerated approval, we have to start that engagement early in order to identify intermediate clinical endpoints, and identify surrogates that can be used. And so since we are not recognizing the utility of it until, at all, very late in the process, we lose that--we forfeit that opportunity.

So thank you, Congressman, for recognizing that.

Mr. {Griffith.} All right, I appreciate that. I would ask you to put on your thinking caps. I don't necessarily expect an answer today, but if you can think of what other legal barriers are out there that are currently limiting the potential for doctors, researchers, drug companies, to communicate on how therapies are working for patients in the

real world, and what can we do to break down some of those legal barriers that are preventing reasonable and valuable treatments from getting to the patients. And if you have an answer today, I would be glad to hear it. Got about 2 minutes of my time left, if you want to use it. If not, if you could submit ideas for the record, I would greatly appreciate that.

Mr. {Sasinowski.} Well, Congressman--

Mr. {Griffith.} Yes, sir?

Mr. {Sasinowski.} --one thing I am not sure about the legal--even though I am a lawyer, I am not sure about the legal impediment. I will have to think about this further, but many of the members of this committee have suggested issues that where natural histories or registries could be a very valuable tool. If we understood more about the natural history, progression of a disease, we could better understand how it might work in a small population. We could be able to discern what is the treatment benefit, versus what is the natural course of disease, and in the same way, we can tell, separate what is a safety signal that is a true safety signal that might be due to the therapy, from just a signal that is

part of the natural course of the progression of the disease.

So these natural histories and registries are very important. We, on behalf of NORD, have been encouraging the development of them in every area, and there are difficulties in trying to get physicians and trying to get medical institutions to be able to share information, and to be able to have uniform information so that we are not talking about apples and oranges. We need some sort of common lexicon in these areas.

So I don't have the specific answer of what are the legal aspects of that--

Mr. {Griffith.} Right.

Mr. {Sasinowski.} --but I know what the target should be.

Mr. {Griffith.} I appreciate that.

Mr. Chairman, if anyone would like my time. If not, I yield back.

Mr. {Pitts.} The chair thanks the gentleman.

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

Mrs. {Ellmers.} Thank you, Mr. Chairman, and thank you

to our panel for being here today on this very important issue.

I represent the Second District of North Carolina, and in our district we have 70,000 veterans, and I am very proud to represent them. Many of them are returning home from Afghanistan, and certainly have come home from Iraq, and living in our communities with PTSD, and I know that is something that you are all aware of. I understand that new path-breaking technologies are emerging in treating veterans with PTSD, specifically, the use of magnetic resonance therapy.

Do you know, and this--Dr. Neil, this is a question for you, do you know if the Department of Veterans Affairs has looked into any of these new technologies, in particular, into the magnetic resonance therapy treatment?

Dr. {Neil.} Thanks, Mrs. Ellmers. No, I do not know that.

Mrs. {Ellmers.} Okay. There again, getting into the issue of how we need to move forward on many of these treatments, you know, such as PTSD. In the, you know, there is broad agreement that the, you know, the present system

that we have with clinical trials is ineffective and costly. There was a--an expert that participated in the PCAST report that estimated a more efficient clinical trial system could cut the cost in half across the industry.

Dr. Neil, do you have any thoughts on what we can do to make trials more efficient and less expensive, and what would this mean to the R and D budgets across the industry?

Dr. {Neil.} Well, thank you again. First of all, I would just say that it would have a huge impact because more than 40 percent of industrial R and D expenditure is in the area of clinical trials.

Mrs. {Ellmers.} Um-hum.

Dr. {Neil.} And one of the reasons that we formed TranCelerate Biomedical as an industry collaboration was to address clinical trials' inefficiency, and there, we looked at this and said these are areas where we do not have, cannot really realize any competitive advantage, and we are all spending the same money over and over again to basically reconstruct a clinical trial's--

Mrs. {Ellmers.} Um-hum.

Dr. {Neil.} --infrastructure every time. We are all

using the same investigators, we are all training the investigators, and then we are not recognizing each other's training. We all have our own Web site to communicate with--so on and so forth. And so we took that on, and the early results are very promising as a way to be able to increase a lot of efficiency, reduce the burden on clinical investigators--

Mrs. {Ellmers.} Um-hum.

Dr. {Neil.} --and reduce the cost. I think there are a lot of other great examples, the cystic fibrosis example being one of them, with their clinical trials network where specific--or disease-specific networks could be created, so you become plug-and-play by being able to start these trials very quickly, and this new lung cancer master protocol, I think, is a great innovation in that direction.

So taken all together, I believe there is an enormous amount of efficiency on the table. There are a lot of things in my testimony that I specifically recommended around IRB's, safety monitoring boards, clinical trial networks, and new innovative approaches to this like, again, in your state, the Duke Clinical Research Institute, their collaboration with

the NIH--

Mrs. {Ellmers.} Um-hum.

Dr. {Neil.} --with the collaboratory. So they are exploring ways to be able to randomize using electronic health records and test different therapies. I think we need to explore all of that, and there is no doubt that we will have the greatest impact on accelerating these cures to patients, reducing costs, and making the whole system work better if we could take that on. And I think Congress could do a lot here.

Mrs. {Ellmers.} Thank you, Dr. Neil.

Let me see, time. About a minute left.

Dr. Tunis, I have a question to--and it gets back to the issue that has been asked a number of times on, you know, how much of the patient involvement is taken into account, especially in the FDA, when it comes to moving forward in an accelerated fashion. What, you know, how does--and--how does the FDA view the patient input on some of these issues?

Dr. {Tunis.} Certainly aware that there is a, you know, a couple of focused initiatives going on at the FDA that are really trying to enhance the degree to which patient

perspectives are taken into account. There is the patient focus drug development that I believe came out of the FDAMA was--and FDASIA was--okay. And then on--in the--actually, in the Center for Devices, there is a medical device innovation collaborative that is very much focusing on patient perspectives on benefit risk, very much with the notion that, you know, one of the potential delays in product development is what level of concern, or what willingness patients have to tolerate risk, and whether the regulatories and the regulator's perspective on that is different from the patient's. And I think there is a view that the patients are probably--are--maybe, in many cases, willing to tolerate more risk, particularly in serious and life-threatening illnesses.

So it seems to me, you know, from my observations, that there is a lot of recognition that the patient perspective is important, and the difficulty is, you know, capturing it both, you know, individually and aggregately, and how do you make a regulatory process that might even have to be adjustable based on individual patient preferences for balancing benefits and risks. So their interest is there, but I think it is complicated.

Mrs. {Ellmers.} It is complicated, and, you know, certainly liability plays into all of this as well.

It looks to me, you really want to comment on this.

Mr. {Sasinowski.} I do. I do, because--

Mrs. {Ellmers.} I would like--

Mr. {Sasinowski.} Because Congress deserves a great deal of credit, and as the lawyer understands the drug law, a 1906 drug law was created, it never mentioned--no law until FDASIA ever mentioned patient. It was assumed that laws could be created in order to enable a regulator to look at what the medical industry and the drug industry produced in some sort of paternalistic way for patients.

Mrs. {Ellmers.} Um-hum.

Mr. {Sasinowski.} Now I am speaking on behalf of NORD, who represents 30 million Americans with rare diseases. And so we are so pleased that this Congress in FDASIA introduced the concept for the first time that the patient voice is meaningful, has a role in drug development, and that is why you had the patient focus drug development, the structured benefit risk ratio. The FDA said we can now empanel--the FDASIA law said empanel patients in part of the FDA internal

review team as special government employees. Tiffany House with Pompe Disease did that for a drug for Pompe, and the FDA reviewers, later when I talked to them, I said what did you learn from having a patient for the first time as part of your internal review team? They said we learned that for a patient with a relentlessly-progressive deteriorating disease, that for that patient to be stable was a huge win.

So the role of the patient is now emergent, and it is due to this Congress. So I just couldn't avoid taking the time to say thank you.

Mrs. {Ellmers.} Thank you to the panel. And thank you, Mr. Chairman, I know we went over our time, but I really could not avoid hearing those thanks and appreciation words. So much of what we typically do not hear. So thank you.

Mr. {Pitts.} The chair thanks the gentlelady. And thank you for your remarks.

The chair recognizes Mrs. McMorris Rodgers 5 minutes for questions.

Mrs. {McMorris Rodgers.} Thank you, Mr. Chairman.

Would any of you, and maybe specifically Ms. Radcliffe or Dr. Neil, speak to the bureaucratic or regulatory burdens

faced in starting or conducting clinical trials? And when was the last time that we, as a nation or Congress, addressed the regulatory framework which governs how clinical trials are conducted, and do you think it is time for an update, given new technologies we can now bring to bear?

Dr. {Neil.} Yes, I do think that this is an important issue, as I said previously, which is impacting the speed of development and its cost, especially, and also its effectiveness. So I do think this is worth a re-examination. I think there are a lot of things that we could potentially do at the statutory level. And here, I am thinking about standardized contracts for investigators, institutional review boards, safety monitoring boards which could be set up at the national or regional level, rather than the inefficiencies of having to establish these at every institution, and not having people who are necessarily as professionally qualified and experienced in monitoring these types of studies as they could be, as examples. And I think that working through public-private partnerships, or possibly authorizing additional money through the NIH to allow these trial networks to be established would also be a great help.

Ms. {Radcliffe.} Yes, I recommend Dr. Neil's testimony as a fairly comprehensive list of some of the things that could be done to expedite clinical trials. For BIO specifically, we have launched an initiative to look at 4 things. One is central IRB's, that is to streamline the review of protocols when they extend over multiple academic centers. The qualification process for drug development tools, such as biomarkers, and we have talked a little bit about that earlier in this hearing. Clinical trial networks. One of the great advantages of establishing clinical trial networks is to speed up the patient recruitment process which, today, is very much longer than it has been in the past. And so we could really make great inroads to addressing that issue. And finally, adopting a risk-based approach to clinical trial monitoring using centralized monitoring mechanisms. So those are 4 areas where we really want to make some progress at BIO over the coming years.

Mrs. {McMorris Rodgers.} Thank you. Thank you.

Like many, I have been following the story of an innovative company, 23andMe, which developed a DNA testing kit that allows individuals to see which diseases or

conditions they may have a predisposition to. And it seems to me that alerting individuals that they are more likely to have a certain disease or condition is a good thing, and it could be something that aids the development of new and innovative cures. For example, the genetic make-up of an individual who carries the gene for Huntington's Disease but does not suffer from the symptoms could be analyzed to determine what is his specific biology that stunts the development of that awful disease.

So the question, are products like this making a major step towards personalized medicine and tailor-made cures, and what does it mean for millions of people to be able to have crowd source--to be able to crowd source their genetic information? Anyone that may want to answer.

Ms. {Radcliffe.} All right, I will answer. We are--in the biotechnology industry, we are extremely excited about the potential for the use of genetic information in the design of clinical trials, and the expediting of those clinical trials, and also in healthcare delivery to help physicians and patients understand the best course of action. I think it is also important to understand though that

information needs to be delivered in a way that enables the best decision-making by patients. A very specific example is that a patient might receive information about a risk of a certain type of cancer, and take action on that in a way that really would be detrimental to that person's health. And so as all of this wonderful information comes out, and as it is made available more broadly, we also have to put a great deal of thought toward the context for delivering that health information in a way that is helpful and not harmful.

Mrs. {McMorris Rodgers.} Then would you speak to the role that FDA is playing in the process, and has FDA promoted the development of these kinds of diagnostic test? Is the FDA approval process adequately equipped to consider these types of products?

Ms. {Radcliffe.} This is an area where BIO has worked for a long time with FDA. The products that are coming out are so novel and so different from those that have been reviewed by FDA in the past, that they really require a different kind of scrutiny and different expertise. FDA has done a lot to improve that regulatory process, and to ensure that it has the expertise internally to manage these new

technologies. I think that in the future, there will be a need for FDA to continue evolving to make sure that it is keeping up with the pace of scientific advances.

Mrs. {McMorris Rodgers.} Thank you. And I too want to thank the panel and for everyone for participating. I am very excited about this 21st Century Cures Initiative, like everyone.

Thank you, Mr. Chairman.

Mr. {Pitts.} The chair thanks the gentlelady.

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

Mrs. {Blackburn.} Thank you, Mr. Chairman. And I want to thank each of you for taking the time to be here, and I apologize that we have been jumping up and down from the first floor where we have Chairman Wheeler with the FCC with a hearing going on, and I know for some of your groups, having access to broadband for some of the new medical apps, for telemedicine concepts, things of that nature, is very important. It is important to us also. So we have been in and out of that hearing.

I have been pleased to catch some of the comments about

clinical trials and looking at those meaningful outcomes of bringing patients into that process, and we were discussing this in our office this morning. Dr. Summer, who is--does our health policy in the office, and I were talking about how important that is to have that impact. And my experience, you know, you have health professionals like Mrs. Ellmers and Dr. Cassidy and Dr. Burgess that are on this panel, but I come from the other side as a community volunteer who was chairman of the board for the Lung Association, on the Heart Board, the Arthritis Board, Children's Hospital, those components there in Nashville. And realizing as we put the emphasis on different participation for managing disease like asthma and the outreach we did with the Lung Association, how important it was to hear from those patents and those patients of how different protocols and therapies affected them, and what the outcome was, and the importance of finding something that worked.

And, Dr. Radcliffe, I think it is the reason it was so--when I went to the State Senate in Tennessee, I took the initiative of working with a colleague, and we pulled together a biotechnology task force to begin to look for some

of those personalizations that can come about in the medical field for treating these--the diseases that impact us. So I have enjoyed hearing your comments today, and appreciate that you all would take your time.

Just more one question I want to add to the mix here. And, Dr. Allen, I am going to come to you on this. We have had a little bit of discussion this morning as we have looked at Section 903 in FDASIA, and being able to pull those external experts into the process, and, of course, the conflict of interest, things of that nature, always has been such a problem, but I think that for those of you who are medical professionals, and for those like me who want to find answers and find a way to cure some of these diseases, having that participation is vitally important. And so I would just ask you, how is the FDA doing as it comes to the involvement and making it possible for some of these experts to openly participate, be full participants, in this process, which is what we are going to have to have if we get to some of these answers?

Mr. {Allen.} Right, so I think some of the panelists have already commented on bringing the FDA's efforts, and

bringing patient expertise to the process and how important that is, in addition to Section 903 that you mentioned, bringing subject matter experts into the review process. And I think that was a very important component of FDASIA to expand on activities that the FDA was already doing, and might be able to even enhance through 903, and making sure that there were diverse experts in really subsets of specialties like rare diseases, or in different genetic diseases, to make sure that they had access to them.

You know, again, this goes back to resource-constrained agency. They simply will never have all of these experts, and particularly, as medical therapy becomes more and more diverse and specialized. So I think the--Section 903 provides one way to allow experts to be more involved in review, and I think we all can agree that we would like to see the FDA continue to implement that as rapidly as possible. I think even there is opportunity beyond just Section 903, which is really focused on involving expertise in the review process, but even things with not just the specific review, for things like developing best practices and guidance documents, there is a real opportunity to also

call on those experts and those patients to make sure that they are able to contribute to the many diverse and important things that the FDA is charged with carrying out. And they continue to have more and more responsibility, and, unfortunately, not the resources to go along with that, so this is one way to help open those doors.

Mrs. {Blackburn.} We will continue to hold them accountable. Thank you, sir.

Mr. {Pitts.} The chair thanks the gentlelady.

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

Mr. {Engel.} Thank you, Chairman Pitts, and thank you, Ranking Member Pallone, for holding today's hearing. I am pleased that this committee is focusing its efforts on the 21st Century Cures Initiative, and the President's Council of Advisors on Science and Technology, PCAST, Report, on Drug Innovation.

I believe that some of the best work that this Congress did during the 112th Congress was in working together to pass FDASIA. I have always been proud to serve on this committee because of the tremendous impact laws that originate within

this committee can have on medical research and disease treatments.

21st Century Cures Initiative proves that this committee's commitment to getting new treatments into the hands of patients as quickly and safely as possible remains strong.

So let me ask you, Dr. Neil, in your written testimony, you suggested that Congress target its efforts in several different ways; one of which, and I quote you, was ``to ensure that the FDA has adequate resources to do their job.'' I think it is critical the FDA--that the FDA does have adequate funding and staff resources in place in order to meet the demands of increasingly-complicated and advanced medical therapies. I know there was significant frustration last year when sequestration caused $85 million in pharmaceutical and medical device company paid user fees to be unavailable to the FDA. Fortunately, the fiscal year 2014 Omnibus Appropriations Act restored the ability and the availability of these funds to the FDA. However, beyond funding, Dr. Neil, you mentioned that, and again, I am quoting you, ``new trial designs and clinical endpoints will

require collaborative efforts with academics and patient advocacy groups.''

So could you elaborate on how academics and patient advocacy groups can better assist the FDA with the resources they need to meet the demands of 21st Century medical treatments?

Dr. {Neil.} Yes, thank you very much, Mr. Engel. I believe that FDA should be given more resources so that they can engage consultants, convene meetings with outside experts and also with patient advocacy groups to a greater extent. And I also think part of their--this new resources allocation that they might get beyond their base budget funding could allow them to hire more staff that could engage with small companies along the way to be able to guide them through the process more efficiently. I think they don't have enough money right now to be able to support the sort of scientific work that they need to do, in other words, there could be a lot more scholarship and original research in the areas of regulatory science that impinges on all of this inside the FDA, both an intramural and extramural program, and also the ability, just simple things like being able to travel to

scientific meetings, I know that that is constrained right now too. And all of these things would help them to be able to create a more scientific culture internally, to be apprised of the latest advances in science, and to be able to incorporate that as they need to in their review process.

Mr. {Engel.} Well, thank you.

I mentioned to Dr. Woodcock during our last FDASIA hearing in November 2013, but I am particularly interested in the development and approval of drugs for rare diseases. I am a co-author of the Paul D. Wellstone muscular dystrophy community assistance, research and education amendments of 2008 and 2013. I did it in conjunction with our colleague, Representative Burgess, and one of the aspects of FDASIA I am most interested in is the improvements made to the various expedited approval pathways, and the establishment of the breakthrough therapy pathway. To me, diseases like muscular dystrophy are why the expedited approval pathways are so important. One type of muscular dystrophy, Duchenne Muscular Dystrophy, is the most commonly lethal genetic disorder of children worldwide, affecting 1 in every 3,500 live male births. There is no cure, it is always fatal, and often at a

young age, so the best hope for those with Duchenne is to treat the symptoms and delay its progression. However, in recent years, the muscular dystrophy research pipeline has held much promises, potentially life-saving therapies appear on the horizon, some of which are a result of Congress' efforts to improve research into this spectrum of muscle-weakening diseases through the MD Care Act, which was first passed and signed into law in 2001.

So it would appear to me that establishing quality intermediate endpoints that can add value to future trials is vital for experimental medications to be considered under the various expedited approval pathways.

So my question is recognizing the significant challenges that exist in developing therapies within the rare disease space, how can the FDA, NIH, drug companies and patient advocacy organizations better work together to ensure proper parameters for success and failure, being established through the critical trial process? Anybody want to comment on that?

Mr. {Sasinowski.} Well, Congressman Engel, I couldn't applaud you more for your work in the area, and with the MD Care Act and others, for reaching out to these communities of

patients with rare diseases. So thank you for your work in that area.

I think that my testimony--my written testimony, I tried to describe what I thought would be four proposals that would advance the interests of those with rare diseases. I think number one is, you know, to again have FDA use accelerated approval more often. As I noted in my written testimony and my oral statement earlier, that when we looked at all of the use of accelerated approvals since FDA started it for the AIDS crisis in the mid-'80s through June 2013, there were only 19 drug therapies that the FDA had approved with that pathway that were not for cancer and not for AIDS. So it has to be used for these rare diseases, because in these rare diseases, we are looking, just as you said, Congressman, we are looking for something--an endpoint in a trial design that is something short of the ultimate clinical benefit. We don't want to have a clinical trial that is going to follow DMD boys all the time until they lose ambulation. And that is the ultimate clinical benefit, and we don't have the luxury to design clinical trials because we don't have enough boys and we don't have enough time. So we need to establish

these other endpoints, and I think accelerated approval would help us do it, and I think this committee has done a great deal in FDASIA, and I think that there is more though that can be done.

Mr. {Engel.} Thank you.

Thank you, Mr. Chairman.

Mr. {Pitts.} The chair thanks the gentleman.

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

Dr. {Cassidy.} I am sorry, I came in late, so if someone has already answered this. Several of you, and I think the PCAST recommendations speak of increased NIH funding, and decry the fact that since '03, there has been some decline. And reality is we have constrained federal resources.

So with that context, there was an IOM report or GAO, I can't recall, from about 20 years ago suggesting that the NIH should reprioritize its funding priorities, and better reflect current needs. Frankly, I think when I looked at it a couple of years ago, they had not done so.

Now, do you have any thoughts on whether or not the NIH

is appropriately allocating its resources to our current funding needs? I look at Alzheimer's, I think it may be getting $600 million, but the cost of future Alzheimer's is huge.

Ms. Radcliffe, do you have any thoughts, just to call upon you?

Ms. {Radcliffe.} First, thank you for highlighting the importance of continuing to fund the NIH. As you noted, the real--

Dr. {Cassidy.} Yes, I got that, but--

Ms. {Radcliffe.} Yes.

Dr. {Cassidy.} --frankly, we don't have enough money. So my real question is, my pointed question is, does the NIH need to reallocate some of its assets, because, again, the IOM suggested this 20 years ago, I am not sure it has been done since.

Ms. {Radcliffe.} Yeah, so we have been extremely supportive of a new center at NIH called the National Center for Advancing Translational Sciences, NCATS, and we are extremely interested in supporting the work of that center--

Dr. {Cassidy.} I--

Ms. {Radcliffe.} -- because it will more directly lead to--

Dr. {Cassidy.} I hear what you are saying. I have limited time so that is not really what I am asking.

Dr. Neil, any comments upon what I just suggested?

Dr. {Neil.} I think they are doing a very good job, actually, in prioritizing at the moment. One wishes that one could predict where important discoveries were going to come from, but--

Dr. {Cassidy.} Now, let me ask you, it isn't so much to predict important discoveries, it is the fact that we have this incredible challenge of neurodegenerative diseases. I mean that is just out there.

Dr. {Neil.} Right.

Dr. {Cassidy.} And if you look at what we are funding that with relative to other diseases and their future cost, which is easily predicted, it seems perhaps, again, a different priority than others would select if you could just start over. So any specific--again, people may be hesitant to criticize NIH, but if we are asking for more funding, we have to also know they are using their funding wisely.

Dr. {Neil.} Yeah. I just wish that one could, again, really think about how to prioritize and manage it, but we don't know where a discovery in a completely different area that affects mitochondria or who knows what may be the breakthrough that we need in neurodegenerative diseases.

Dr. {Cassidy.} You are suggesting that we need to have no direction whatsoever, I think I am--I think is what I am hearing from you, but rather rely upon kind of basic research to produce.

Dr. {Neil.} Well, I don't think it is just that, but I think that the most promising basic research needs to be funded if we are going to continue to advance.

Dr. {Cassidy.} Mr. Sasinowski, any thoughts?

Mr. {Sasinowski.} Yeah, it--with your particular concern about neurological, neurodegenerative diseases, yeah, a large swath of the rare diseases in this country fit into that category. And as, you know, Dr. Neil just mentioned, you know, the underpinnings, the pathophysiology of many of those go back to mitochondrial energy production. So if we could have reallocation of NIH funds that would redirect it to some of these areas that have the promise of being able to

address a lot of diseases, that might be a worthwhile endeavor.

Dr. {Cassidy.} It seems like we should have some metric; what is the future cost, what is the current morbidity, and have it reflect that.

Dr. Tunis, you know, I used to do medical research. My nurse who I worked with, who basically told me what to do when I showed up, said, man, the paperwork has increased dramatically over the years. Now, one of the recommendations, I think number seven, suggests that maybe FDA could be more efficient in terms of how it does it process. I am asking you just to ask, it could be anyone, how would you grade what FDA has done in terms of, is the monitoring process thoroughly useful, or is some of it kind of, oh, my gosh, why in the heck are we doing this? It is just driving up cost. Any kind of a--any kind of grade you would give the FDA for their current efforts?

Dr. {Tunis.} Well, I think--I would hate to grade FDA, but I think FDA actually recognizes that there are a lot of this excessive activities and cost embedded in clinical trials, and one of the things, again, Garry and others know a

lot about is they do have this partnership with Duke called the Clinical Trials Transformation Initiative which is systematically trying to identify where there are, you know, excessive regulatory burdens, things that contribute to the inefficiency of clinical research, and, you know, doing--you know, exploring how those things could be minimized. So I would give the FDA an A grade in terms of identifying that there are opportunities to improve, and having at least that forum to, you know, to look for solutions. And I don't know if, Garry, you wanted to add anything to that.

Dr. {Neil.} Well, the--monitoring is a particular issue that we took on with TranCelerate, and FDA provided input into that, and we know that we are overdoing this in ways that are not really adding value, maybe subtracting value and driving cost, so moving to a more risk-based monitoring approach, again, with FDA--

Dr. {Cassidy.} Any sense of how much cost that adds? Five percent, 10 percent, marginal cost of--

Dr. {Neil.} It--

Dr. {Cassidy.} --monitoring which may be inefficient?

Dr. {Neil.} It depends on the trial, obviously, but--

and I can't give you a precise estimate, but it is very substantial.

Dr. {Cassidy.} Very substantial.

Dr. {Neil.} Very substantial.

Dr. {Cassidy.} Okay. That was kind of my impression from being frontline way back when.

Thank you very much. I yield back.

Mr. {Pitts.} The chair thanks the gentleman.

That concludes the first round of questioning. We are going to go to one follow-up per side now.

I will recognize Dr. Burgess 5 minutes for his follow-up.

Dr. {Burgess.} Thank you, Mr. Chairman, and again, I want to thank the panel for being here. It has been a long morning but a very informative morning. I would be remiss if I did not acknowledge, I guess, my co-sponsor, Eliot Engel, has left, but the MD Care Act, Mr. Chairman, that is a good Bill and one that I hope we can have a legislative hearing and a markup on before we get too deep in the political season, because it is one that needs to occur, and, in fact, the last reauthorization--we haven't addressed the problem

that occurs that we are doing such a good job, some of these patients are now living until early adulthood when they didn't before, and the current Act does not address young adults with the illness, and we need to do that. So I hope we can have that legislative hearing.

I also, Mr. Sasinowski, I don't want to correct you, but it was actually the last Congress that passed FDASIA, but it was this committee that did the work, and I just wanted to acknowledge the work of Brian Bilbray, who is no longer with us, and really it was his--I mean he was a bulldog on the surrogate endpoints when FDA was in testifying before this committee. And without Brian Bilbray's contribution, I don't think FDASIA would have been as effective, and, of course, the--I certainly--I appreciate the hearing this morning about the conflicts, the trying to improve the status of the conflicts language so that we could improve the advisory panels that we empanel to advise the FDA on approvals.

Look, one of the things that the President's council did come up with and talk about was the woeful state of the information technology at the Food and Drug Administration. You hear the urban legends about the warehouses of new drug

applications that are in boxes on paper applications in the basement somewhere. I don't know whether it is true or not because I have never seen it, but can anyone speak to--I guess there has been the hiring of a new chief information officer. Does anybody see any daylight on the horizon there? Apparently not.

Let me just tell you what is so frustrating. This committee, for the last--I have been on the committee for 10 years, and we have had this discussion over and over and over again. As a practicing physician, I have received the slings and arrows because doctors' offices are not coming into the information age rapidly enough, and here we have the FDA which is just stumbling all over itself. I mean surely there is something we can do about that to digitize the data. I mean if this were a class action lawsuit, the large litigation firms around the country would get together, digitize the data and analyze it in a weekend, and we can't do it as a federal agency. I don't know, surely somebody has some thoughts on how to improve this system. Again, let the--for the clerk's benefit, no one volunteered an answer. I just--I acknowledge this is something that needs to be fixed.

I appreciate Dr. Cassidy's comments about the funding constraints, but if we don't fix this, we are not getting out of this problem.

I do want to ask Mr. Sasinowski, probably the one thing I have heard this morning that I am going to take with me out of this hearing is that perhaps the default position that the FDA ought to be the accelerated pathway. And the FDA historically has been risk averse, but you are talking about a new world order where the FDA now defaults to the accelerated pathway. So can you speak to accelerated approval as the default in the future?

Mr. {Sasinowski.} Yes, Dr. Burgess, that the--I don't see it as a default. I don't see most of the therapies coming through the FDA's gauntlet, being approved under accelerated approval because it only fits for those which are serious diseases where there is an unmet medical need, but what I am saying is that those twin criteria could apply to many diseases, especially the rare diseases, the 7,000 rare diseases that affect Americans, and so for those, you know, that should be part of the discussion at the beginning, at the pre-IND meeting, when we are first coming into the FDA,

that should be part of that engagement, because you have heard several other witnesses, and it was also in FDASIA and PCAST, that said if you are going to go forward with accelerated approval, you have to start that discussion early because you have to be able to identify the surrogate endpoints, and the intermediary clinical endpoints so that you can run the studies in the proper way. And so that discussion is not going on. So what I was suggesting, Dr. Burgess, is that every time that a new therapy is proposed to the Agency, one of the first questions always be, as part of their checkbox, is this a candidate for accelerated--would this fit, is this a serious disease for which there is an unmet medical need, and then the system can integrate that. And it is currently just not being considered.

Dr. {Burgess.} Not only is it not being considered, but I will just tell you, not a month goes by that someone is not in my office with a tale of woe--

{Voice.} Yes.

Dr. {Burgess.} --about getting their drug or device approved, and I am--I for one, in this committee, I am just tired of hitting my head against that wall, and it is time

for us to break through or break out of that modality and move into the 21st Century.

Thank you, Mr. Chairman, for holding the hearing. I will yield back.

Mr. {Pitts.} The chair thanks the gentleman.

That concludes the questions at this point.

The Members will have follow-up questions. We ask that you please respond promptly.

This has been a very informative hearing. We appreciate you sharing your expertise with us and the practical recommendations.

I remind Members that they will have 10 business days to submit questions for the record. Members should submit their questions by the close of business on Tuesday, June 3.

Without objection, the subcommittee is adjourned.

[Whereupon, at 12:10 p.m., the Subcommittee was adjourned.]