UNITED STATES OF AMERICA

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

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CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

MEDICAL DEVICES ADVISORY COMMITTEE

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PATIENT ENGAGEMENT ADVISORY COMMITTEE

+ + +

October 11, 2017
12:30 p.m.

Hilton Washington DC North
620 Perry Parkway
Gaithersburg, MD 20877

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DEBORAH CORNWALL, M.B.A.	Committee Member
FREDERICK DOWNS, JR., M.B.A.	Committee Member
BENNET R. DUNLAP, M.S.	Committee Member
AMYE L. LEONG, M.B.A.	Committee Member
SUZANNE SCHRANDT, J.D.	Committee Member
MONICA W. PARKER, M.D.	Committee Member
KATHERINE D. SEELMAN, Ph.D.	Consumer Representative
ROSE BLACKBURNE, M.D., M.B.A.	Industry Representative
LETISE WILLIAMS	Designated Federal Officer

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Private Citizen

MICHAEL SERES
Founder/CEO
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M E E T I N G

(12:33 p.m.)

MR. CONWAY: Great. Well, thank you very much. I'd like to go ahead and call this first meeting, the inaugural meeting of the Patient Engagement Advisory Committee, or the PEAC as it's referred to, to order. My name is Paul Conway, and I serve as the Chair of the Committee. I also serve as the President of the American Association of Kidney Patients in my volunteer capacity, and on a personal level, I'm a kidney patient who's managed kidney disease for the past 36 years, including 2 years on dialysis and for the past 20 years as a kidney transplant patient.

What I'd like to do is read into the record, I think, here at the outset, something that's pretty important. You can see it online, but just so that it's a matter of the transcript.

The purpose of the PEAC: The Committee provides advice to the Commissioner or designee on complex issues relating to medical devices, the regulation of devices, and their use by patients. The Committee may consider topics such as Agency guidance and policies, clinical trial or registry design, patient preference study design, benefit-risk determinations, device labeling, unmet clinical needs, available alternatives, patient-reported outcomes, and device-related quality of life or health status issues, and other patient-related topics. The Committee will provide relevant skills and perspectives in order to improve communication of benefits, risks, clinical outcomes, and increase integration of patient perspectives into the regulatory process for medical devices. It will perform its duties by discussing and providing advice and recommendations in ways such as identifying new approaches, promoting innovation, recognizing unforeseen risks or barriers, and identifying unintended consequences that could result from FDA policy.

I think it's fundamentally important to reference that as we go forward. This is our inaugural meeting. I think if you take a look at the national trend over the past several

years, we're at an interesting juncture point for government, for providers, for investors, but especially for patients. In the national lexicon now, we have many different terms that we use. We use PCORI, we use PROs, we use PPI and many other terms, and all of that, in essence, is the drive to have more patient voice included, and this is why this is fundamentally important that we focus on this Committee and understand why it's so unique.

With the Food and Drug Administration, they're the front line for making certain that patients are safe. And for those patients that are in the room and for those who are involved in providing devices for patients, I think all of us would recognize that none of us would be here today had it not been for the courage of those who came before us in each of those sectors, but especially for patients. And that's the unique thing, I think, about the FDA's efforts here with the PEAC. And I think, on behalf of the Committee, we would like to thank the FDA for providing this opportunity for patients. I would like to express my appreciation to FDA employees for their civil service, for their decision to serve the country and the patient community.

And there's one thing going forward that I think you can expect from the PEAC based on my initial discussions with my fellow members here, and that is this, that you'll hear a lot of different terms about devices, you'll hear a lot of different terms about government and process. But at the end of the day, I think what undergirds everything that we do and everything that we discuss is this: that we understand that the journey of a patient and the desire for people to improve their lives, but especially those who come after them who may be afflicted by the same type of condition or disease. That's what the basis of our thinking is; it's for the betterment.

And, again, I'd like to say thank you to the FDA for modeling what it looks like, and to many audiences that are out there, other government agencies, the public, whether you're

joining us in person or online, to investors, to manufacturers, to citizens that actually care about if their government is responsive, I would take a look at the PEAC today and going forward, and hopefully, we'll be an inspiration for you. Thank you very much.

With that, what I'd like to do is go ahead and turn and have the respective members of the PEAC introduce themselves. I'll go ahead and start with you, Dr. Parker.

DR. PARKER: Monica Parker, Emory Alzheimer's -- excuse me. Monica Parker, Director of Minority Engagement, Emory Alzheimer's Disease Research Center.

MS. SCHRANDT: Hi, I'm Suz Schrandt. I'm the Director of Patient Engagement for the Arthritis Foundation and personally have had a form of rheumatoid arthritis for 27 years.

MS. LEONG: Okay. Am I on?

Thank you, I'm on. My name is Amye Leong from Santa Barbara, California. I'm President and CEO of Healthy Motivation, a communications consulting service. I am spokesperson for a United Nations health initiative called the Bone and Joint Decade. I am chair at the local level of the Arthritis Foundation in Central California. I am an ambassador to the Patient-Centered Outcomes Research Institute, and I am a person who has now 19 joint replacements, a lot of stents, and a lot of metal plates to keep me walking. Delighted to be here.

MS. CHAUHAN: I'm Cynthia Chauhan, a patient representative. I am following Amye, and I don't have quite as many joint replacements as she, but we're working. I have multiple comorbidities. My focus in my advocacy and volunteerism is I'm bringing the patient voice to the research table early in the process, from the time that they first begin to think about what they want to do through actualization of the trial and onward.

MR. DOWNS: Good afternoon, my name is Fred Downs. Currently, I am a prosthetic consultant for the Paralyzed Veterans of America. I retired from the VA after 38 years in

the Army. I was in it 3 years, and I was the National Director of Prosthetics and Sensory Aids Service for the VA for 30 years. I'm currently involved in two clinical trials, one NIH concerning CLL, chronic lymphatic leukemia, and then the robotic arm developed by DEKA out of DARPA.

MS. CORNWALL: My name is Deborah Cornwall. I am a volunteer with the American Cancer Society and its advocacy arm, the Cancer Action Network. I am myself a 16-year breast cancer survivor. I have written a book based on interviews with over 100 cancer caregivers and so have some perspective on cancer and its impact on patients as well as the impact of clinical trials on them. I've also served on two research grant review panels, one at the national level and one currently at the regional level in New England.

MR. DUNLAP: Good afternoon, my name is Bennet Dunlap. I'm an advocate for people with diabetes. Two of my four children live with Type 1 diabetes, and like 30 million or so other Americans, I'm struggling to keep my Type 2 diabetes in control. Actually, I'm trying to keep it pre-diabetes, but it takes work. So I'm thrilled to be here.

DR. SEELMAN: Hi, my name is Kate Seelman. I'm a Professor Emerita and Associate Dean, University of Pittsburgh School of Health and Rehabilitation Sciences, retired last year. I served on the National Council on Disability and directed the National Institute of Disability and Rehabilitation Research, and I'm involved in NSF Engineering Research Centers. And I'm very pleased to be here and look forward to hearing from all of you.

DR. BLACKBURNE: Good afternoon. I'm the Industry Representative for the Committee, Dr. Rose Blackburne. I'm Executive Medical Director at PPD, Pharmaceutical Product Development, a global CRO. Prior to industry, I was a practicing physician and a PI, so I always keep top of mind in working on clinical trials, planning and strategizing clinical trial enrollment, and I'm delighted to be here today.

MR. CONWAY: Thank you all very much. I note for the record that the nonvoting

members constitute a quorum as required by 21 C.F.R. Part 14. I'd also like to add that the committee members participating in today's meeting have received training in FDA device law and regulations.

At this meeting, the Committee will discuss and make recommendations on (1) the challenges for patients and medical device clinical trials; (2) how patient input and engagement is being used to overcome these challenges and potential solutions; and (3) the top areas for FDA to consider for action.

Instructions to the audience. For me, I would ask you to do this: If you've not registered outside, please go ahead and do that as soon as you can and sign in the attendance sheets. They're on the tables by the doors.

I'd now like to introduce Ms. Letise Williams, the Designated Federal Officer for the Patient Engagement Advisory Committee. She'll make some introductory remarks, and I can tell you this, she is a great DFO. Go right ahead.

MS. WILLIAMS: Thank you, Mr. Conway.

I will now read the FDA Conflict of Interest Disclosure Statement. The Food and Drug Administration (FDA) is convening today's meeting of the Patient Engagement Advisory Committee under the authority of the Federal Advisory Committee Act (FACA) of 1972. With the exception of the Industry Representative, all members of this Committee serve as special Government employees. Members and the Chair of this Committee were selected by the Commissioner of the Food and Drug Administration or their designee. They are knowledgeable in areas such as clinical research, primary care patient experience, and healthcare needs of patient groups in the United States, or are experienced in the work of patient and health professional organizations and methodologies for eliciting patient preferences and strategies for communicating benefits, risks, and clinical outcomes to patients and research subjects.

The purpose of today's meeting is to discuss and make recommendations on the topic of patient input into medical device clinical trials. This meeting provides the opportunity to bring patients, patient organizations, FDA, industry, and other medical and scientific experts together for a broader discussion on the important patient-related issue. Those discussions are exclusive of any particular product or class of products, and we will not seek advice on a regulatory decision or action. Therefore, this meeting does not involve deliberation, decision, or action that is focused upon the interest of a specific party or a discrete and identifiable class of products. And, accordingly, it has been categorized as a meeting involving a non-particular matter.

Dr. Rose Blackburne is serving as the Industry Representative for clinical trial design, conduct, and analysis, and she is acting on behalf of all related industry. She is employed by Pharmaceutical Product Development, LLC.

A copy of this statement will be available for review at the registration table during this meeting and will be included as part of the official transcript. Thank you.

But before I turn the meeting back over to Mr. Conway, I'd like to make a few general announcements.

Transcripts of today's meeting will be available from Free State Court Reporting, Incorporated.

Information on purchasing videos of today's meeting can be found on the table outside the meeting room.

The press contact for today's meeting is Stephanie Caccomo.

I would like to remind everyone that members of the public and the press are not permitted in the Committee area, which is the area beyond the speaker's podium. I request that reporters please wait to speak to FDA officials until after the committee meeting has concluded tomorrow, October 12th.

If you are presenting in the Open Public Hearing session for today and have not previously provided any electronic copy of your slide presentation to FDA, please arrange to do so with Mrs. AnnMarie Williams at the registration desk.

In order to help the transcriptionist identify who is speaking, please identify yourself each and every time that you speak.

For the record, FDA has received two written comments, which are provided to the panelists, and a copy is also available at the registration table.

If anyone in the audience has questions or needs assistance, please see an FDA staff member. FDA staff members are wearing name tags.

Finally, please silence your cell phones and other electronic devices at this time.

Thank you very much.

Mr. Conway.

MR. CONWAY: We will now hear remarks from Dr. Jeff Shuren. He's the Director of the Center for Devices and Radiological Health.

What I'd like to ask the public observers at this meeting is to keep in mind that while this is a meeting that's open for public observation, public attendees may not participate at unless at the specific request of the Committee Chair. Thank you.

Dr. Shuren.

DR. SHUREN: Good afternoon. Jeff Shuren, Director of the Center for Devices and Radiological Health, U.S. Food and Drug Administration.

First of all, I'd like to welcome everyone to the first meeting of the Patient Engagement Advisory Committee. I'd also like to send regrets from Dr. Scott Gottlieb, our Commissioner. He had planned to be here today to give remarks. Yesterday he was notified that today he would have to be speaking with folks from Capitol Hill on hurricane recovery, so I will be speaking on his behalf and my behalf. Let me also, on behalf of

Dr. Gottlieb and myself and the rest of the Agency, say thank you to all of the people who are participating in this meeting, for everyone who is here today, for those who are participating by webcast, to also thank all the members on the Advisory Committee for being willing to serve in this capacity. We are very excited about today. Today has been a long time in the making and a long time coming.

What I'd like to do over the next few minutes is talk a little bit on the background of kind of how we got here, why we're here, and some of the other work that's being done at the Center for Devices and Radiological Health around patient engagement. And they'll kind of all go into three buckets, kind of talking a little bit about how we better understand the perspectives of patients and incorporate that into our decision making, how we engage with patients and some of the things that are changing, and then some of the challenges we have with clinical evidence, and that brings us a bit to today's meeting.

For us, patients are at the core of what we do; they are the heart of our mission to protect and promote public health. For us, our job number one is to improve the health and the quality of life of patients, and it's for this reason that we intentionally made the very first role of our vision patients, and that patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance first in the world.

That is not about a competition between countries. It is not about beating Europe. It is not about throwing technologies out onto the marketplace. It is a recognition of the dual aspects of our mission to protect public health by assuring that devices are high quality, safe, and effective, but also to promote public health by facilitating device innovation and timely patient access, because we know that if we have good technology, it is of limited value to patients if they don't have timely access. And in many cases, there can be a tension between those dual aspects of our mission, and it's one of the things that we are always challenged with at FDA: Where is the right place to draw the line for when

technology comes to market in a responsible way, deal with those issues of patient safety but also timely patient access, and at the same time, when product is on the market, address the same considerations as new safety issues should arise.

Now, patients have been an important part for the FDA, and we have tried to include patients in our decision making, but quite frankly, the opportunities for patients to engage are very, very limited. So you think about a meeting like today or other public meetings, we give a chance for the public to weigh in, but people get 2 or 3 minutes to say something, and it's just the nature of the challenge of holding meetings. We open up a public docket, and you can provide comments, but how many people actually read the *Federal Register*, right? We need to go through it, but that is a holdover. The world has changed for how we should be communicating with people.

We have Advisory Committees, roughly 18, oftentimes around product decisions, and we'll have one patient representative. What's so unique here is this is the first time we have an Advisory Committee that is comprised of patients, by patients, and it's for patients. Very unique. The first time at the Agency.

Other opportunities: We do meet with patients at the FDA, groups of patients or groups that represent patients. We also appreciate people can't afford to come to the FDA. They can get on the telephone; that may be not the same. And we don't have the resources to travel around the country to talk and engage with people. So one of the things that we need and are trying to address, maybe an opportunity for a future Advisory Committee meeting is, what are the ways we should be looking at to better interact and engage with patients and get people's input?

One of the hallmarks of decisions that we make for a product to come to market and to stay on the market, when new issues arise, is a benefit-risk determination. For many years, the Agency never articulated how they make those decisions. We said we need to

address that. In 2012 we put out a final guidance that provided the factors we use in benefit-risk determinations in support of product approvals.

And then we went beyond that and started to put out policies about how we use that in decisions around approving clinical trials and then for product availability postmarket when new safety or quality issues should arise. And that's the first time the Agency ever did that, and we included in that, as one of the factors, the preferences of patients, because when you make a benefit-risk determination, identifying there are benefits and risks, and then you're weighing them, that's a subjective determination.

And historically, it was my staff who used their values in making a decision, and we said, well, if devices are being used on or in patients, then quite frankly, we should be taking their perspectives into account. The challenge, of course, is if you just ask people, you get a wide range of opinions. So is there a way to more scientifically assess people's perspectives so that then we could rely on that in our decision making?

And we kicked off an effort in 2014 on trying to advance what's called the science of patient input, a very nascent scientific discipline. As part of that, we developed a policy that we put out in 2015 about considerations if you're going to conduct a study on patient input and how that could get factored in to our decision making.

And complementary to that, the Medical Device Innovation Consortium, a public-private partnership whose mission is to advance regulatory science for medical devices, put out a framework on patient benefit-risk, as well as a compendium on methodologies that could be used to assess patient preferences and the pros and cons. And we have been trying to encourage a variety of entities to conduct those kinds of assessments where we better understand what are the tradeoffs that patients are willing to make and understanding that even in patient populations, it stratifies, and starting to look at what are the differences in subpopulations, what is most meaningful to patients?

One of the things we did is we worked with RTI on a structured survey that was given to about 600 individuals with obesity regarding benefit-risk tradeoffs in obesity treatments. The result, we changed our framework for how we think about those technologies, and in 2014 we approved a device for the treatment of obesity. It's the first time we had approved a device for obesity since 2007, so 7 years of nothing. Since then, about six other products have come to the market, and it's a very healthy pipeline, and that's all because of patient perspectives and taking that into account.

Just a few weeks ago we cleared the first device that was based, in part, on a patient preference study conducted by the company. This was the NxStage System One home hemodialysis device, and it had been on the market for use at home with the patient and a caregiver, and what we were hearing is an interest about could that be used just by the patient and no caregiver because for some people it's not viable to have the caregiver engage for their times and need home hemodialysis given. And we had a very good survey that had looked at perspectives, and in fact, yes, many of the patients understood the tradeoffs involved and thought that that was acceptable, and we knew the technology had the right safeguards in place that it could be used appropriately in the home setting, and so we expanded its indication.

But we also used patient preference information to improve the safety of the technology, the Dexcom 5 continuous glucose monitoring system and Animas Vibe system, a combination of a continuous glucose monitor and an insulin pump, was intended for children. But there was concern from the parents that we were going to tease out regarding unintended boluses of insulin. And so we worked with the company, as a result, to put in a lockout feature to avoid that.

So here are cases where we started with "Let's make a change in how we do business." We put out policies, working with the community. Now studies are being done

sufficiently robust, we can rely on it, and that is now driving access to technologies but also safer technologies.

We've also been looking at how we can better understand and measure what matters to patients. So we've had an effort under way on how we can better use and make sure we have qualified patient-reported outcomes, and over a 5-year period we saw an over 500% increase in the number of pivotal clinical trials for PMAs that used patient-reported outcomes, and now over 50% of the PMAs include patient-reported outcome data.

And in the reauthorization for the Medical Device User Fee Act, we're now for the first time getting resources to build out a patient engagement group at CDRH. Prior to that, believe or it not, there were never dollars that had been allocated to us specifically for this kind of work. Now, for the first time, that's going to occur.

We've also been looking at other opportunities for how we engage with patients, and for the past few years we've had a big focus on customer service because we moved from saying the people we deal with are "stakeholders"; they're our customers. I even get reports, and I have to cross out "stakeholder" and write in "customer." So everyone is, people outside and inside the Center.

And all of our staff get trained on customer service, and you can rate us on your customer satisfaction, and we get the results, and we change what we do based on the feedback.

But we also recognize our number one customer is patients and that how we engage with patients has to change, much like the role of patients have changed from simply passive recipients of what a clinician wants to do, to advocates for care, to consumers of information with the rise of the internet and personal computers, to now an interest in shared decision making on where we think the next stage is, truly our partners in the work that we do, and that's why, for the past few years, a strategic priority has been patients as

partners, partner with patients.

Just the other week I was at a conference. I had a young man who had a spinal cord injury, paralyzed below the neck due to a diving accident, and he found his way to Ohio State University and had been working with them. He was their subject, if you will, test subject on a technology for the brain telling the muscles how to move, and now, with his thoughts, he's able to use his hands and his arms, he can drive, he can pick up things, all from new technology. But he said, you know, I am not a research patient; I'm a research partner. I found that very compelling and dovetails very well what we're trying to do at the Center.

But to get there, one of the first things is not just how do we understand, through science, people's perspective; we have to immerse ourselves. And so we made a commitment that all of the staff at CDRH, 100%, would have had the opportunity for engaging with patients at least once by the end of this calendar year. We kicked that off in 2016. We are now at over 85%. We've held over 30 events with roughly 50 patient organizations, and we felt that it was so important that it's not just the people who review products, it's just administrative assistants who answer the phone or respond to an e-mail have to understand and have the perspective. And when we surveyed our staff, over 90% thought that those interactions were relevant and informative to the work that we do, and we have people who have engaged in multiple events and want more, and we're going to bake that in as an ongoing activity for the Center.

We also had a Network of Experts for scientists and clinicians. We have now built that out. We have a Network of Patients, patient groups, where we now can call on -- identify and call on people in the patient community to help us in the work that we do. And that also led us to PEAC, because one of the other things we committed to do is to set up this Advisory Committee as another mechanism for engagement with patients.

And then, finally, clinical evidence: Clinical evidence is a challenge. We often rely on traditional clinical trials, but the problem is they can be very resource intensive, time consuming, costly. In addition, oftentimes, because of inclusion/exclusion criteria to conduct the studies, they may not be reflective of the full range of patients who would use that technology in clinical practice, let alone the clinicians who would use it, and therefore many times a premarket clinical study will not give you the true benefit-risk profile for a device. And also, for more uncommon events, I'm not going to identify that -- in some cases, hundreds to thousands of patients who participate, which you can't do.

And then when we kick some of the issues over to the postmarket, a lot of challenges conducting studies postmarket because patients lack the incentive to enroll and particularly given some of the designs for clinical trials. So this also brings us today, how do we better incorporate the perspective of patients in the design of clinical trials, so rather than designing it around the needs of the investigators, designing it around the needs of patients and their lifestyles? How do we do things like make better use of technology to maybe pull information while people are in the home setting? Are we measuring the things we should be measuring? And if we can do that, then maybe we get to more and more robust clinical trials.

But at the same token, we know that if we really want to understand and get a full understanding of what a technology does, we need to study it when it's out in routine clinical practice. And data is collected all the time in clinical care, but it may be of poor quality, incomplete, different systems measuring different things, so we can't make good systematic use of that data today. So we've had another effort under way for the past few years, a strategy we put out in 2012 to establish a National Evaluation System for health, with a small h, Technology, or NEST, about how we sort of use the marketplace to drive towards higher-quality, lower-cost use of real-world data and get a richer understanding of

what technologies do, their impact on patients, clinician use.

In addition, if we can deal with larger datasets, we can address another challenge we have, which is the safety net that exists here not only in this country but most other countries. So, today, if we want to identify is there a safety problem, we're often relying on passive surveillance. That means a human being, usually a clinician, identifies a problem, makes the connection that they believe it's associated with a device, and takes the time to report it. And as a result, safety issues may be missed, or it may be a long time before they're identified, and many more patients are exposed to that device than otherwise would need to be. But with larger datasets and use of analytical software, we can move towards more of an active surveillance system complementary to the passive support reporting and have a much more robust safety net here in the U.S.

In setting up NEST, we said this cannot be an FDA system. It's got to be of, by, and for the ecosystem. So it is now operated by an independent coordinating center, which is the Medical Device Innovation Consortium, to help get it up and running, and it is governed by representatives from the various, what we'll call customer community, the stakeholder communities, in the medical device ecosystem. So it is not just simply practitioners and government; it's also payers, it is industry, but it's also patients. And part of the role for this governing committee is then to build out for forums and opportunities to engage their respective communities, and that means bringing patients more into the fold so that as we are building NEST and we are using and thinking about the use of real-world data, we're doing it in a way that also best meets the needs of patients.

With that, again, I will say thank you to all of you for coming. Today and tomorrow we're going to hear a wide range of perspectives. That's one thing we have learned. There are people all in various places regarding technologies and its benefits, but also technologies and the harms that they've caused to people. How will we account for that in

the work that we do? How do we make sure that that voice for patients is incorporated, and not just incorporated, that patients themselves are our partners in the work that we do?

So, again, thank you to all of those who have come, and thank you to the Advisory Committee.

MR. CONWAY: Thank you, Dr. Shuren. And I think especially, thank you for recapping the strategic vision that you have, that your team has, and that with the support of the Commissioner is clearly dedicated now into reforming a process, but just as importantly, accompanying it with results and measures. And as a patient community, I think we appreciate that.

Next, we'll hear from FDA in a presentation on clinical trials and medical devices by Dr. Owen Faris.

DR. FARIS: Good afternoon. My name is Owen Faris, and I'm the Director of the Clinical Trials Program at CDRH, and I'm really excited to be here today. I want to just echo a lot of the comments that Jeff said. You know, this is really an exciting day for all of us in the Agency, and my hope today is that I can give you a little bit of an inside view in terms of what goes on in the Agency, who we are, how we do our work, and how patient input could have a really important role going forward.

So this slide is one that's often the first slide in a lot of talks that I give, and I know Jeff uses a nearly identical one, and I just knew he would scoop me today and basically say what was on this slide. But what better meeting than today to have this slide as our first slide to talk about why we're here and why we do what we do and how it really is focused on patients? And I'd like to focus on a few parts of our vision statement there. The first part is -- and I think folks are very comfortable and aware about and when they think about FDA, they think about that we are protecting the public and making sure that devices that

go onto the market are of high quality, they're safe, they're effective. And what I think folks might not think about quite as often is that it's also important to get those technologies to patients as quickly as we can.

And if I can just diverge on a personal note for a moment. You know, as is the case with any large diverse organization, many of the folks that work at FDA are patients ourselves who rely on medical devices every day, and I'm one of those patients. As a longtime Type 1 diabetic, I think about the impact of blood glucose meters and their evolution, and when I was handed my first blood glucose meter in the early '80s, it was nothing short of a miracle. You know, I could be home or at school and check my blood sugar.

But there were patient issues with that device that made it difficult to use. It took several minutes to use, it took several complicated steps that had to be done at certain points along the way. It was messy. It wasn't discreet. And as a teenager trying to fit in and, you know, have a social life with my peers, I'd rather just have my blood sugar be high, and that's what I did, and I used it very rarely.

Flash forward 30 years, and now I look at my phone, one swipe, and instantly I know exactly what my blood sugar is. Not only that, I know what it was 5 minutes ago, 10 minutes ago, 20 minutes ago, and that gives me a pretty good idea of what it will be 5 and 10 and 20 minutes from now. I know my blood sugar today like I know the time of day, I know it all the time, and it's life changing in terms of how I manage my disease, and that's the sort of experience that many of us bring to the work that we do.

So let me start off by talking about some of the differences that we see between devices and drugs. Many of us are familiar with the large clinical trials that we expect to see in drugs. There are reasons why our device trials often look different. So a few of the key points here: One, devices are often highly dependent on the clinician knowledge, their

experience, their skill in terms of how they're implanted, all of the elements of using that technology.

We also see devices be iterated upon. We see new devices that are groundbreaking and change things dramatically when they're introduced, but the nature of most device development is iterative improvement upon previous generations of devices. And we see that even during clinical trials themselves. You know, we learn from the patient experience, we learn from the physician experience, and things get changed during -- you know, very rapidly. There are new iterations of devices, and we have to adapt to that.

And so for many reasons, the gold standard of a randomized controlled trial, while we do see that in some device studies, there are many studies for which that just isn't practical.

So there are opportunities. Jeff talked about many of them already. First is that we need to be an agile organization that knows that we can't always get all of the information we'd like to have about a particular condition, a particular device, but if we think about it, if we look at it, and if we talk to folks like patients and physicians and the companies, and we think about, well, what is it that we really need, that's our entire least burdensome principle. What is the minimum dataset that you need to answer the questions in order to have it be reasonable to put a device out on the market?

There are lots of tools, and I'm going to talk about a few of them a little bit more in the coming slides, in terms of modeling and adaptive designs and use of real-world evidence that are really part of the future of clinical trials that can make them much more informative and efficient.

And we are in collaborations. Jeff already talked about the National Evaluation System for health Technology. We worked very closely in getting that off the ground with industry groups, patient and clinician groups. These kinds of interactions are essential to

the kind of work that we do.

So when we're thinking about innovation, there's a lot that's changed just recently in this space, and even if you look over the past couple of years, a lot of it is highly relevant to what we're talking about today, so innovating patient preference into our clinical trials and our decisions about regulatory submissions, thinking about ensuring that clinical trials are sufficiently diverse to represent different ages and races and ethnicities, using real-world evidence in our decision making and adaptive designs. These are efforts that are ongoing today that show that we're really moving toward the future with clinical trials.

And so if we think about the typical sort of standard way that a device might get to market, let's think about a high-risk Class III device where we might start with preclinical testing, a lot of preclinical testing, thinking about biocompatibility and sterilization and mechanical testing and all of the relevant testing that would support bringing a device to market, depending on what the benefits of that device are and what its risks are.

That then leads us into the company, the sponsor, making the case that we're now ready to do a clinical study, and FDA reviews all of the data in support of the proposal to conduct that clinical study: What testings were done on that device before the study starts? What is the study going to test? Who's going to be enrolled in that study? Are the right precautions in place to protect patients in that study? Is it appropriate to enroll patients shortly, frankly, in that study? And is the study going to ask the right questions? Is the study going to have the right endpoints that answer questions that would be relevant to us assessing the safety and the effectiveness of that device?

So let's move on to the next step. That study is completed, and we see a premarket application. Now we're talking about, well, now we have this entire dataset, it has premarket, it has postmarket -- preclinical and clinical data, and we're trying to decide are the benefits and risks such that this device should be on the market and should patients

have access to it?

After we get through that step, there's generally a postmarket assessment, and we're going to continue to learn from this device and ensure that the patients are protected, that things are functioning well out in the world. And this has been sort of a traditional, relatively simple linear view of how devices get onto the market, and now I'm going to complicate it a bit.

So now we're talking about the real world, and how we can better use data that are happening, that are being developed in real time out in the real world. So a device enters the market on the far right there, and now the real world hits, and that clinical trial focused on a focused patient population, certain conditions, a certain disease set, it had a limited number of patients and now things are expanding. Physicians and patients will learn how to use that technology in slightly different ways. There will be data occurring in real time. And the mission for the Agency now is to figure out how do we learn from that and make sure that we're using that information as best we can. So, at times, that information may be so robust that we say, you know what, here is a limited indication for this device, but now we have this robust real-world data that can support an expanded indication for that device because it's being used in a broader way, into a broader set of patients, and it's working.

There might be other times where the information that's derived from that experience informs a design of a new device or a modified device, and it generates a hypothesis, that we then start that cycle all over again.

And another important element of this is, as this information is generated, if we can assimilate it, if we can put it together in a cohesive, understandable way that can be used to inform the decisions that patients make, that physicians make, and so those devices will be even safer and more effective going forward.

So we have a lot of regulations that govern how we conduct the trials. I'm not going

to go through them in detail today. The one that we talk about the most is 812, so that's our Investigational Device Exemption regulation, so that's what we commonly call an IDE. That is the clinical study for an unapproved device or a device that isn't approved for the use that it's being studied for. And for a company to conduct that clinical study in the United States, if it's of significant risk, they need approval from the FDA to do that. And so there's a set of regulations for governing how we make those decisions. We work with sponsors of those studies to inform those decisions. We want to make sure that the studies are safe for patients, that it's reasonable to expose patients to those devices in the context of a clinical study, and we also want to see and make sure and provide feedback to the sponsor about whether that study is designed appropriately to ask the right questions.

Part 50 is informed consent, so that is -- you know, it goes hand in hand with 812. When we're looking at a clinical trial, we look very closely at the informed consent documents and the process to make sure that patients are well informed about what they're signing up for in a clinical investigation.

Part 54 is financial disclosure of investigators.

Fifty-six is institutional review board regulations, so again, hand in hand with protecting subjects. The IRB has a critical role to play here ensuring that subjects are protected.

And 45 C.F.R. 46 is the Common Rule, that's what it's commonly known as, but it's a set of regulations around human subject protection that are broader than FDA regulations but are highly related, and FDA looks at those regulations in consideration for how we shape our own.

So we think of regulation as something that's static, and in large part it is, but there are changes that happen to regulations and some of them that happened relatively recently. Here's just a few. So there have been some major updates to the Common Rule

that have impact for how clinical subjects, clinical patients, are studied in clinical trials, and that is having an impact across the clinical research space. FDA recently released a guidance document about waiving informed consent for certain clinical trials that couldn't be conducted practically with informed consent and are of minimal risk to human subjects. They have very specific criteria for why those would -- you know, why those studies are appropriate and how patients are protected in them. But this is an important move forward, and eventually, it will be replaced by a regulation that catches up to that guidance document.

And very recently we had a change in the law to allow central IRBs for device trials. Prior to last year, all clinical trials for devices had to have local IRBs for every clinical site for those clinical trials. We now can allow central IRBs, and in fact, in many cases we're really encouraging them because we think this is an efficiency step that can really help improve clinical trial enterprise.

So when we think of the primary groups that are involved in a clinical trial, we have FDA, we have the sponsor, we have the IRB, we have the investigators, and you see sort of the biggest cog here is the patient. And it's also, you know, we don't see the whole cog here, and I think, you know, that that's representative of the situation. We have some insight into what patients are thinking or what they feel and their preferences, but we don't have the whole picture. And if you take anything from my talk today, it's that I hope you'll hear that we're making progress but that there's more to do, and that I hope that you and the advice that we hear from this group and the discussion over the next couple days will help us get there.

So just very briefly, let me just talk about who are we in CDRH. So we have a lot of engineers -- I'm one of them -- biomedical, mechanical, electrical. We love to look at the designs of devices and understand how they work and understand how they're going to be

tested, and we give a lot of feedback about the nonclinical elements of testing.

We have a lot of clinicians, and this is not a complete list of the kinds of clinicians we have, the specialties that we have, but it gives you an idea that most of our review teams, and certainly any review team that's looking at a clinical trial application, would have at least one or more clinicians on that team.

We have other scientists and specialists, so chemistry, toxicology, software, microbiology, animal studies, just to name a few. These are folks that are looking very deeply into the testing in support of that device, either to allow it into a clinical trial or to allow it onto the market afterward, ensuring that it's been studied safely and that it's safe to put into patients or be used with patients.

We have a lot of statisticians, epidemiologists, informaticists that are really helping us look at data, understand the data, making sure that our questions are being asked in a way that preserves the integrity of the study, and these folks are an important part of our review teams.

And we have folks that specialize in regulatory issues, compliance, program support, quality.

So this isn't everyone in CDRH, but it gives you an idea of a lot of the folks. And as I mentioned, you know, many of us are also patients, but we still don't have what I would say is an adequate voice in every situation where a patient perspective would be really helpful, and I'm going to go through just a couple of scenarios that might give you an idea.

So here's a boardroom, a conference room. The bat phone in the middle is key because we often have folks on the phone in our meetings, too. This could be a meeting that is just an FDA team; we've reviewed a clinical trial application and we're trying to decide what to do. We have 30 days to make that decision, and that's not a lot of time. This team has come together after they have reviewed the submission for a couple of

weeks, and they each have ideas about some of the challenges. These are people that are represented by the boxes from my previous slide, and they all have the questions and challenges, and they also want to see this technology move forward, if it's appropriate to do so.

So here's just an example. We're here trying to decide what to do about this clinical trial, and a question comes up: Are the right patients going to be enrolled in this study? So this could be, you know, are the enrollment criteria appropriate, you know, to enroll the right patients? But it could also be, you know, how is this study designed to make sure that we'll get a sufficiently diverse population that will be a patient population that is not just the enrollment criteria fit the patient population but that the study will actually enroll patients that fit the population of interest?

Will the trial measure outcomes that matter to patients? So, you know, this is a key point that we've been talking about already quite a bit today. We want the trial to be gathering information that's relevant to the patients that are going to be impacted by the use of this device.

Will patients be willing and able to adhere to the follow-up visit schedule? So we may design the perfect trial that's going to gather exactly the kind of information we all need to answer this question, and if patients have to come back too frequently or have to drive too far or spend too much time in the hospital or do something that's really burdensome, we may get a lot of missing data in that trial and get inconclusive results. And, so again, thinking about what is the patient experience going to be in this trial and how can we find the right combination of getting the data that's necessary to make the decisions that need to be made, but also making sure that we're conducting a trial that's practical for patients.

So coupled with that is are there ways the trial could be modified to be less

burdensome for patients? These are the kinds of conversations that you can't have without having patients in the room or in the discussion, and we don't do that enough, and hopefully today will be the start of us, you know, moving even further into that direction.

Do patients understand the potential risks and benefits? Part of that is reviewing the consent form and the process, but thinking about, you know, what's going to happen in this trial to make sure that patients are on board with it, they're signing up for and is it going to be acceptable.

And, lastly, does study success equal patient success? And what I mean by that is, typically, a pivotal trial that's going to be the primary clinical data to decide whether a device should go to market has primary endpoints. Usually there's a safety endpoint and then an effectiveness endpoint. And that, in our minds, generally constitutes if you -- if the hypotheses are met, then the study was successful, there was study success. And so a question here is does study success translate to how a patient would view success for this device? And this is a key question that we need to be asking ourselves and figuring out how do we get to the right answer there.

So I'm going to give you one more slide that looks like this. Now, fast-forward a year or two, and we have a marketing application. The clinical trial has been done, and we have a team here. This could be the same team. It could be a team that has some folks from the sponsor there, the manufacturer of the device. We're having a conversation about the data that are in front of us from this clinical trial.

And so think about this as just one of many different questions that could come up. Here's a question from the reviewer, and it says some patients experienced a certain adverse event at a higher than expected rate. Should we still approve the device? We have some variation on this question every day, all the time. The data are never perfect, right? We have things that happen differently from what we expected. We have missing data at

times, we have patients who couldn't complete follow-up, we have different ways in which the data are not perfect. And yet, if we waited for the data to be perfect, we wouldn't meet the other part of our mission, which is to get devices to patients in a timely manner so that they can actually benefit from them.

And so a question comes up: Are there mitigations that can be put in place to address this risk?

Are the benefits highly meaningful for patients, right? You can look at the risk without the context of the benefit and say is this risk acceptable? Well, it depends, right? It depends on the condition; it depends on what we saw in terms of the benefits.

And, again, we'll turn to the patient view: How do patients view this risk in the context of their disease and their treatment alternatives? If there are five or six other devices that treat this condition very well, they have good alternatives, well, then we might look very closely at this risk and say we need to overcome this risk before this device hits the market. On the other hand, if this is a very sick, serious condition and there aren't good alternatives, we might say, well, this risk is suboptimal, but for now this is the best thing for patients is to label this risk, to talk about this risk, to see how we can best mitigate it and to bring this device to patients.

So when we talk about those sort of things, we think about other tools that we have in our toolbox, and one of them can be postmarket tools. And so can we think about -- can we continue to learn in the postmarket? Can we study it closely? Can we be ready to respond if the performance is unacceptable? These are the kinds of questions that factor into that decision. So it's difficult to make these decisions, and we will be making them even better if we have a stronger patient voice in the decision-making process.

So we know these conversations happen all the time. The problem is that there is, at times, a disconnect between what happens between the patient and their physician and

what happens in one of those rooms when we're having the discussion about what to do. And we really want to break down that disconnect, and the idea is that if we can bring patient perspective into that conversation, we can have some light bulbs go off, and we can be much more informed in our decision making. And conversely, if we can convey better in a two-way conversation what's happening in those discussions and why we got to the decision we did and what we see is the value of this device and what we might be concerned about and what we want to look for going forward, we can have better informed decision making.

So I have just two more slides, and I just want to review a couple of points. One is that not all patient information is the same, and that's okay; we have a lot of different reasons why we might need patient information in the first place. And so patient preference information, I think we all know, is very important in figuring out what do patients want and framing the questions that we're asking.

Patient-reported outcomes is a key part of many of the studies we see. These are data that are in a clinical trial, and they're being reported by patients in those trials. I will say that not all patient-reported outcomes are patient focused, and not all endpoints in a trial that are patient-reported outcomes aren't patient focused. That's a lot of negatives. But my point is that we can derive important information directly from patients, and that can be important.

We can also derive clinical information that's not gathered directly from patients but that is very important information that patients care about.

So high-quality surveys is one way that we can get some of that information, figuring out how do patients see the benefits of this device. How do they view the risks?

Patient organization engagement could be very important. Medical professional engagement, care partner engagement, and patient focus groups.

So there are a lot of ways in which we can get information that can help inform our decision making with regard to what patients care about, and depending on the kind of question that's in front of us, it may need to be a higher grade than other kinds of questions. We're thinking about how do we make this trial practical, and what do patients care about? That might be one level of information that we want to derive. If we're thinking about should we put this device on the market, what do patients feel about the benefits of this device, the risks of this device, we need to be pretty confident that we can rely upon that data as being representative of the patient group.

So this is my last slide, and I just want to walk through. This is just another version of the typical life cycle of a device, where we start with an idea. We iterate upon it in terms of developing that device.

We do some preclinical testing to figure out is it ready for prime time in terms of bringing it to patients and testing it clinically? That testing is very extensive, and there's a lot of discussion with the Agency during and after.

Then we move to a clinical trial. That clinical trial could be successful, and we could go forward with a regulatory marketing application, or it could dial into new ideas if it moves to the left there, where you have a regulatory submission where we're making a decision as to whether to have that product enter the marketplace. There's a product launch and postmarket.

And if we start by thinking about, you know, where could the patient voice be helpful here, the last message I'd like to leave you with is, kind of everywhere and the earlier the better. So, you know, we might be most familiar with understanding the patient perspective and having -- it's not an accident that these arrows are two-way; this is a conversation that we're talking about. We might be most familiar with having that conversation at the end; the device is on the market, we want to understand what's the

patient experience, how is it working out there in the marketplace? That's helpful information. But wouldn't it be even better if the patient were engaged when we're making the regulatory decision in the first place, and we're using information from patients to understand should we allow this device onto the market, given the benefits we're seeing, given the risks we're seeing, given some of the uncertainties we have? How does the patient feel about the decision that we're contemplating?

Wouldn't it be even better if the patient were involved in designing the clinical trial to gather that data in the first place? It's great if we can take patient information and inform our regulatory decision at the end, but wouldn't it be better if the trial that gathered that data in the first place were designed with patients in mind so that the questions at the end of the day, patient success equals study success, all are moving in the same direction?

And it doesn't stop there, in my mind. When we're thinking about preclinical tests, I mean, we have to be -- we're trying in some way to simulate the patient experience, we're trying in some way to simulate what's happening for that device and understanding what will be the patient experience, what could be the patient experience, what they are experiencing in their lives that we should seek to overcome, could be very informative to designing better preclinical testing before we even enter the clinical trial.

And, lastly, wouldn't it be even best if we could be engaging with the patient at the very beginning when we're thinking about what technologies need to be developed in the first place?

So thank you for being here and thank you, for the audience, for being here as well. Again, we at the Agency are very excited about this meeting, and we look forward to a productive discussion.

MR. CONWAY: Thank you, Dr. Faris.

(Applause.)

MR. CONWAY: And especially for sharing how your own patient experience informs your professional outlook. We appreciate it.

Next, we'll hear a presentation from Duke Clinical Research Institute.

MS. PATRICK-LAKE: Thank you. Hi. So I am Bray Patrick-Lake, and I am the Director of Stakeholder Engagement at the Duke Clinical Research Institute, and before that, I was the Director of Stakeholder Engagement at the Clinical Trials Transformation Initiative, and I will largely be speaking to you about that body of work related to patient engagement today.

But first, I wanted to start off with what is perhaps the most important slide in my deck, and that is the disclaimer. So you'll see that this slide notes that my views and opinions do not tend to reflect those of Duke University or CTTI. The reason is because I have been a patient rep for FDA since 2009, and we have a huge shift going on today. This is the most fun Advisory Committee meeting I've ever been part of. I've served as the patient rep on a variety of them. Mr. Conway and Ms. Williams, I may try to bring it down a little about let's talk about regulations and what we have to do, but this really is a day to celebrate.

For so long, as a device patient -- and I'm a particular connoisseur of implanted cardiac and vascular devices. I've been attending meetings and not been able to connect with people that had a mindset for what we could do for device patients. We've been aggregated by disease and body part. I think in the past we've come together around, you know, drug development activities or particular policies that we are trying to develop, but it has been very hard to actually put together a device community, and just seeing you all sitting in front of us today is very exciting to me, in particular, as an individual patient.

So I am going to skip this slide because it's only going to get me in trouble. I tried to list out all the great things we've done to change culture. Dr. Shuren and Faris have already

been through much of that, but I just want to point out that things really are changing. And so on the Rogers model from 1962 of innovation, we know that there are innovators, there are early adopters, there are early majority, there are late majority, there are laggards. And we really have gotten to that point, the tipping point, in cultural change for acceptance of patient engagement in the device space. How do I know that? Owen Faris and I have similar slides, which is kind of scary, but I also know we've made a big change towards what's important to patients. I don't just think it's Stockholm syndrome because you are a nice guy, but this tells me we've actually made some really incredible changes.

Through the work of MDIC, MDEpiNet, and now we've got NEST, and we see that patient groups are constantly being included in governments. We see that we've got people here today, and I've seen Edwards and Abbott, who are doing patient preference studies, which was actually hard in the early days of patient-centered benefit-risk to find groups that were willing to actually engage as demo projects. And now that we've got that happening, we also now have a vice president of patient engagement with Edwards with us today. And so that tells me that we are starting to actually really shift and really walk the talk of what we've been talking about.

So shifting into the project I'm going to speak to you about, the Clinical Trials Transformation Initiative, is an FDA public-private partnership to improve the quality and efficiency of clinical trials. It is a multi-stakeholder organization because we know that it is important to bring all of the different perspectives together from patient groups, industry, academia, government, regulators; we all need to sit around the table and figure out these problems.

I'm going to leave the depressing part about why CTTI formed to Ken Getz, who's going to follow me with all the statistics about how we're failing in clinical trials, where we have low and slow enrollment, people are dropping out regularly, and we actually have

investigators pulling out of research, but there's never been a better time for us really to focus on improving the quality and efficiency of clinical trials, and that is exactly what CTTI has been doing.

So CTTI is an evidence-based organization, and I just want to give you a brief overview of the methods. We're bringing stakeholders together to identify the problems in the clinical trial enterprise, and it is set about in a rigorous method of gathering evidence, seeking solutions, refining ideas, and then, most importantly, propelling us all to action. So armed with their evidence, we can actually go out and drive adoption of practices because it's not enough to create evidence, we also have to actually work on the uptake.

So CTTI was formed in 2007, and we've always had patients at the forefront, but in 2013 we really started increasing our patient membership because we really understood the power of patients in driving improvement in the clinical trials enterprise. So as we started seeing some nascent partnerships in the clinical trials enterprise, particularly with patient groups, you know, we had a willingness to start engaging, but yet there was a gap in knowledge and understanding about how and when to engage, who to engage, how do we actually engage, and do that in a way that's both productive and legal. We were thinking about a regulatory environment. There was really, in 2014, a paucity of empirical evidence. We had a lot of anecdote, we had a lot of good mom and apple pie, but we really didn't know how to best engage, and there were no actionable recommendations.

So CTTI started off with a project, the longest project name in history, Best Practices for Effective Engagement with Patient Groups around Clinical Trials.

And this is the project team. You'll notice that it is multi-stakeholder. It started as a smaller group, and then as work streams were added, it grew over time. But, most importantly, all of the various perspectives of stakeholders have always been brought together to solve these problems as a group.

So CTTI started with a literature review that we actually didn't even publish because there was so little to it. We had a lot of great literature, and we had, again, not much of anything; there were some things about good communication, transparency, sharing information, but we really never got to the nuts and bolts about how to engage around clinical trials and actually documenting some of the activities.

So we set out with the literature review, and we moved on to a survey. Then we went on to some semi-structured interviews with sponsors, investigators, and academia to understand how patient groups are engaging in the clinical trial enterprise.

We also wanted to understand what were the barriers and what were the successes and what were the failures and then come to consensus around actionable recommendations about how we could have more efficient and successful clinical trials through partnership.

So CTTI undertook the survey in 2014. CTTI also worked with the Drug Information Association to get that out to our stakeholders. CTTI does have device companies that are members, but I will tell you, we actually have a hard time finding folks engaged in the device space to actually take the survey. So we did have a small number of respondents, but again, it wasn't a very representative sample, and it would be fun to actually -- I keep using the word "fun," which maybe I shouldn't, but this is fun. We should actually do the survey again and see if we could get even greater interest from the device community.

We moved on to stakeholder interviews to really kick the tires and understand some of the perceptions and the different interactions that were going on and the successes and the failures.

And then later in 2015, we had a multi-stakeholder expert meeting where we unpacked all of the evidence, we had a lot of dialogue, a lot of great -- to really look at, you know, what these experts had to say about consensus around different recommendations.

So this slide is really important because when we did our survey initially, you'll see that the majority of the interaction with patient groups, between sponsors and patient groups, was actually going on at a Phase III clinical trial. So file this number away, I'll come back to it later, but it's very important that you don't see in the discovery phase in the preclinical a lot of the work actually going on in that area.

We also elicited through this work a lot of barriers to collaboration, and then we confirmed those through our semi-structured interviews. But you will see that we have a variety of things from internal resistance and lack of buy-in on the sponsor's part, to patient groups just getting a token seat at the table and not really being full partners in the process. We had a lot of mismatched expectations. There were perceived legal and regulatory challenges to working together, lack of demonstrated value. Partnerships could be really disparate, and so if you didn't know who to engage and how to engage, you might not have a great partnership on the end of that. In some cases there were lack of sophistication of patient groups was actually noted, and it's very important to understand each patient group.

In CTTI's work, we use patient group as kind of an all-encompassing term and as a conduit to individual patients. So I don't want you to think that because this work focused on patient groups, we're not talking about actually engaging individual patients in our work, but we had to have those honest brokers and kind of the entity to actually engaging the patient voice to elicit through our surveys and our research.

But a lot of people basically were unsure of how and when to engage, but the most important thing that we learned is that all the barriers we elicited were modifiable, and that is extremely important. So we built this continuum of the different activities that patient groups were engaged in across the clinical trials enterprise, starting from pre-discovery and going to postmarket. And, again, Owen, you're scaring me a little, but you've talked about

all of these different things where we should be bringing people in to talk about the inclusion and the exclusion criteria. Is it a meaningful clinical endpoint? The patient-reported outcomes, we did hear a lot, too, that patient-reported outcomes are often physician reported outcomes and not actually what's most important to the patient, and so we really need to do that type of work with the patient community. You'll see that we've got patients that are serving not only in the protocol design phase, advising on recruitment and retention strategies. All of this is really the goal of minimizing the burden on the patient and maximizing the value for both patient and sponsors.

It's also more common that we were able to document that we've got patients serving now on data safety monitoring boards and also moving into the postmarket space. And if we're going to start turning the crank and really taking in patient perspective, learning as fast as possible and getting safe and effective products to market and out into the hands of patients sooner, we have to start thinking of this in a more cyclical manner.

So you just saw this slide. I stole this from Katie O'Callaghan's presentation back in 2015, but it's obviously iterated on this now and the CTTI -- you know, the CTTI graphic ends up being muddier, but the truth is, it is constantly going back to the other -- to the beginning and not just dropping off when we get to postmarket; it's the constant assessment of unmet need and then working with patients again to drive this entire cycle of ideation, development, testing, and getting products to market.

So one of the primary upshots of CTTI's work was this goes through active and continuous engagement. Patient groups and partnering them with a clinical trials enterprise does actually produce a unique value and benefit of basically de-risking and also reducing regulatory uncertainty.

So through active, continuous engagement, we do have more effective and efficient clinical trials with a greater chance of success, so the better design of the study questions

and the endpoints. You know, data quality is a huge thing, and I have been on too many FDA panels where we get to the end of the presentation by the sponsor and, you know, there's all lost to follow-up or dropout, and we don't know if those patients are dead, we don't really know what happened to them, but we have to assume the worst. And so it's really important, and we want to make sure we have the best study design as possible, that we know about the barriers up front, that we've actively worked with the patient community to really understand are they willing to accept the risks and the benefits.

So CTTI had -- it's about 25 recommendations. Every time I give the presentation, it's like it's 50. Now it's like 100 recommendations. But no, it's really about 20 different recommendations that are divided out by all stakeholders, sponsors, and patient groups. The results have been published, and they are available free online, and it's a practical guide to how to work with patient groups around clinical trials that are evidence based, and I've pulled out just a few snapshots.

So one of the most important points at the meeting is the engaging early, often, and always. This is the answer to how and when do we engage. It is unfortunate, so I have a better-than-zero model. When you look at, you know, there's engagement around Phase III, sometimes it's true that a project is -- you know, in Phase III it's a postmarket, and we haven't engaged patients earlier. So it's never too late. You should figure out how to start engaging patients in clinical trials, but the earlier you can do it, the greater the benefit.

So we need to include the patient's perspective in the product development. They're very clear about the unmet need, the therapeutic burden that currently exists, the subgroups of patients, and then the perceptions around benefits and risks. I was personally in a clinical trial that was -- for low and slow enrollment, and if you would have asked even three patients, we could've told you, up front, this is what we needed to do in this device trial to actually make it more successful.

And I think I've already spoken to this, but definitely making sure that the protocol is as minimally burdensome as possible.

So when working with patient groups around clinical trials, it's really important that we speak very clearly and even have some type of structure around what we're asking people to do. So that could be an MOU. It could also relate to data sharing. It could also be some types of partnerships and resources, but we want to make sure that people understand how they'll work together, you know, what are the goals, what are the objectives, clarifying expectations.

Also, it's important to understand that when you're working with patient groups around the regulatory process, that the truth is the FDA is the ultimate owner and working out with the sponsor who's going to be the decision maker. So even if a patient group says, you know, we don't want to have a blinded study or we don't want to be randomized, sometimes that's not practical for rigorous science and for the regulatory setting, and so it's very important that you set these expectations and understandings out at the beginning of the project.

Managing the real or perceived conflicts of interest: So it was really interesting, as we talk to sponsors working in the space, some of the barriers to working with patient groups, FDA ruled out. Absolutely not true, and we've heard from the Agency and leadership that it's very important and that we're finding many ways to do it. But it is true, you can't communicate about or promote products off label or promise benefit to products that are still under investigation.

So you do need to manage these conflicts of interest and make sure that appropriate policies are in place. So when you're working with patients, you need to clarify that to them because patients are not very -- not everybody is an expert in this space, and I think patient groups, now that they're engaging more in the clinical trials enterprise, some of the boards

are actually better prepared and have policies around conflict of interest in place. But we really need to make sure that we don't skip that step and that we keep all of the partnerships between the lines.

So ensuring that patients aren't token voices and that they really are essential partners. You know, this is tough. We've seen a lot of box-checking. So you bring patient groups in. Again, Dr. Faris's slide on all the things we should be doing around clinical trial design. Those are actually not as hard to do. If you've never done it, it seems scary. How would I talk to patients about a protocol? How would I talk to them about endpoints? These are scientific words. But that is really where the benefit is. It is not showing somebody a glossy brochure and saying do you like the picture on this? Do you like, you know, the text? It really is working in the clinical trial design phase and ensuring that we do take in those voices. And actually, if you're going to work with people, you also have to have an action/reaction. So it's not enough just to take in their feedback and check the box. You do actually have to respond to that.

I'm not going to stay long on this slide, but I want to introduce the notion of value. So CTTI has gone on in the next -- on the next phase of the project to actually -- we had a conceptual model of value based on expected net present value, which probably sounds crazy from the patient perspective; who cares? But we do care, as patients. We want clinical trials to be successful, and that means answering a question positive/negative/otherwise. So we want to speed this up, we want to stop wasting our resources, and there is a benefit when you avoid protocol amendments and when you have, you know, compliance for the study and you have great data. At the end of it, there is actually a financial value to that.

So, in conclusion, I will just say that partnerships are occurring with greater frequency around clinical trials. The culture, I think we are at a great place, we have moved

the needle, it is starting to tip. We now actually have evidence-based recommendations and best practices, and you can download all of this stuff at CTTI, and it was also recently published in the *Therapeutic Innovation & Regulatory Science* journal in July of 2017, if you would like to read more.

Thank you.

MR. CONWAY: Thank you very much.

(Applause.)

MR. CONWAY: We will now hear a presentation from CISCRP, the Center for Information and Study of Clinical Research Participation.

MR. GETZ: Okay, thank you very much. I'm Ken Getz, and I just want to thank the CDRH and PEAC for the invitation to participate today. I'm actually coming to you wearing two different hats, as an associate professor at the Tufts University School of Medicine and also as the founder of a nonprofit group whose mission is to educate the public and patients about the importance of clinical research in advancing public health. So the goal is really to raise overall public literacy and understanding about research and how it fits into their own treatments and their own care.

As a researcher at Tufts University, we've been monitoring industry practices within primarily drug development for a very long -- over 40 years, and our earliest recollection of patient engagement being discussed among pharmaceutical and biotech companies was about 10 years ago. So we've come up on our 10th year anniversary when patient engagement was first initially discussed, and of course, it took some time for organizations to begin to focus on various initiatives that could be piloted and implemented, and that's really what I'd like to focus on today. What are some of these initiatives that have been implemented, what are the benefits that are being seen, and what can we expect in the future?

Beginning in around 2010, we saw a huge proliferation in the number of patient engagement activities that were being piloted. In fact, these initiatives came from entrepreneurial individuals or ventures, they came from service providers, and they came within companies themselves, and they ranged from so many areas that you've already heard discussed today, these focus groups or patient advisory boards, all the way through to home nursing networks and concierge services, wearable devices to aid the convenience and to improve the experience for the study volunteer or the patient in a clinical trial.

What I would argue is that while we've seen so many initiatives that have been implemented, and many would argue that each one of them has offered a benefit, some have offered far greater benefit than others, and that's really where I would like to direct the Committee and my talk today, to really look at those areas where there's real overlap as a true partnership between the patient and organizations that are supporting clinical research and overseeing it. Where are the places where there's really an overlap where we see the highest relative benefit to the patient community, and at the same time we see the highest relative benefit to the drug development and the device development enterprise, places where we can ultimately see the contribution of patient engagement to delivering the best quality, the safest treatments that can be offered moving forward.

Well, the best place to begin to think about where benefit can most be realized is to look at some of the measures of current conditions today. And Bray had alluded to this. I just want to share some of the metrics that we routinely gather to give you a feel for the challenges that are faced by the drug development enterprise, and we know many of these conditions are also now being experienced by device companies, as well.

The drug development enterprise is enjoying one of the most innovative periods in its history. It has produced a very large volume of drugs that are in development, and that has been fed by a very, very active discovery engine and an innovation engine. But the

process of developing a new therapy is so much longer today than it's ever been before. It's riskier today than ever before. We are now looking at the highest failure rates we have ever seen in our industry. And we also know that the cost to develop a single successful drug or device is extremely high, in part because the successes have to carry the cost of all of the failed efforts as well. So that high risk and the long cycle time translates into very, very high cost in addition to the large out-of-pocket investment that has to be made.

In the work that I've done at Tufts University, we have found that the number one cause, the root cause for so many of the conditions that we face in developing a new therapy relate to the design of the protocol itself. The scope of our studies is the largest it has ever been. If you look at just the number of endpoints and objectives in our studies, they doubled in number with the highest growth in the exploratory and tertiary and secondary areas. Our primary endpoints and the number of key secondary endpoints has stayed relatively the same.

So the scope of our studies has really expanded dramatically, and we're collecting so much more data to support and provide the evidence that we need to demonstrate not only safety and efficacy but the cost effectiveness, so the economic benefit of the therapy and its value. So much more has to be demonstrated through the data that's collected. And that also translates into many more procedures that have to be performed at every single visit for each study volunteer. The demands on participation are remarkably high.

The very last line of this table captures a very interesting statistic. We know that a higher proportion of all the data that's collected is not really supporting the regulatory submission. It's data that may have value in the future, it's data that may help in interpreting some of the findings, but it's not critical, it's not essential to the core endpoints and objectives of the study. And that's really helped to raise the cost and extend the cycle time of our clinical trials.

One of the interesting findings that we see time and time again is the relationship between protocol complexity and performance and quality. The more complex our studies, the worse our performance and the worse our quality. Today you can look here just at our patient recruitment and retention experiences. On the left-hand side we see, across every therapeutic area today, that we typically have to double the planned enrollment period in order to attract and to retain the requisite number of volunteers to support the objectives of the study. So we have to double the planned enrollment period, and we continue to see growth in that area.

On the right-hand side, you see the typical performance of a community of investigator sites on any clinical trial where 10% of them will be unable to enroll a single patient, in large part because of the incredibly demanding and high number of eligibility criteria, the inclusion and exclusion criteria, and those are increasing, particularly as more of our research focuses on precision medicine and smaller patient subpopulations. So complexity, overall, is expected to continue to rise dramatically.

The area that's perhaps the most alarming is that orange segment in the pie, the proportion of investigative sites that under-enroll. These are sites that are activated and may enroll a single study volunteer, but they fail to complete the enrollment requirements. It's a very costly group that has to be maintained, and often, they will not be able to continue through the full length of the study because it closes before they're able to complete their participation in the program. And often, the patients in those particular sites who may have been screened and randomized into the trial don't have an opportunity to participate.

The last area I want to focus on is now just taking it down to the executional level. In response to the complexity of our protocols growing, we have seen more sponsor companies, pharmaceutical and biotech companies, look to expand the number of sites for

which they're engaging, and they're dispersed across more countries, and that introduces a level of operational complexity, having to work with multiple regulatory agencies and health authorities around the world, the challenge of collecting data and distributing clinical trial supplies to different sites dispersed all over the world.

The number of patients per Phase III study, on average, has actually gone down. It's actually declined. It's one of the only areas where we've seen a decline, and that is in part because we're targeting diseases for which we're looking for smaller populations today than the traditional chronic diseases that we studied in the past.

But also, we note that we're spreading the smaller number of patients across a larger number of centers around the world, and that creates a number of other challenges as well. This is a more disparate community; it's more difficult to integrate the data that we're collecting; it's very, very fragmented, and that creates a lot of delays and inefficiencies as well. And some of the other measures that I show here really capture the cycle times at the individual site level that really demonstrate the burden that our research professionals have to endure in supporting our complex protocols.

Well, there are three primary benefits that patient engagement offers to really improve the current operating conditions, and what they really suggest is that patient engagement may, in fact, be the key to help address these operating conditions that we've been dealing with for 30 or 40 years.

And the three primary areas are the following: The first is focus and relevance, and some of the earlier speakers touched on this area. How do we get our protocols to be targeted and focused on the most relevant and meaningful areas? Where are the endpoints the most clinically meaningful? Where can we actually connect the studies to the patient community that is looking for that research to provide answers and to ultimately deliver a better therapy? So focus and relevance is essential, and that will drive better success rates,

it will help simplify protocol design, and may ultimately help us speed up our studies as we begin to cut out some of the noise that may exist and a lot of that additional scope that we've added to our designs. Relevance also relates to connecting participation in clinical research to the value that we, as a community, place on study volunteers through their gift of participation. What we learn from their participation has value for public health overall and for all of us.

Feasibility, the second area, really relates to understanding how we can ensure that our protocols are more easily implemented, how can we reduce the number of eligibility criteria and the number of procedures, and focus and relevance will help us in that area. But more feasible trials will remove some of the inefficiency and speed up our studies and may also help really lower the cost of a lot of the work that we're doing.

And the last area is convenience, which really relates to providing the most enhanced experience for our study volunteers to ensure that we make it a positive experience and one where they'll want to continue their involvement through the end of the trial.

The chart that I just pulled up really shows you the top areas of initiatives, patient engagement initiatives that are being implemented today, and they really touch on every one of these three areas. The number one area reported by companies this year in a survey is the use of a patient advisory board or boards to provide input into protocol design. And most of the feedback really centers around relevance and feasibility with some discussion as well about convenience, how to make the trial easier for them to participate.

Some of the other areas: the use of professional advisory boards. So soliciting input from study coordinators and from physician-investigators is another very common area.

The return of clinical trial result summaries has become a more widely piloted initiative across a large number of companies as a way of demonstrating appreciation for

the gift that our study volunteers have provided.

And the last two areas, the use of home nursing networks and the use of wearable devices, are the two most common areas where industry is finding benefit in improving convenience and their collection of real-time data. So it's helping to expedite our studies.

It's interesting. We have been monitoring adoption for some time, and what we see are more organizations that are piloting initiatives and a growing percentage that are planning or considering implementing initiatives, but we have not seen any real widespread adoption, adoption that touches a company's entire portfolio of activity or practices that are embraced by the industry as a whole. And I think that relates to some of the comments that were made earlier. We have an environment where there has been an absence of clarity in terms of policy and even regulatory acceptance or direction here. We see a lot of reluctance in organizations given how risky drug development activity has been to disrupt a lot of the traditional legacy processes. And so there is some fear, and that has created a lot of that reluctance to embrace specific initiatives that I think we all can agree are important standard practices that we hope to ultimately achieve.

And I would argue that the return of results to study volunteers is probably one of those areas. We all know it's the right thing to do, we know that the vast majority of study volunteers want it, but the vast majority do not at this time, after they complete their participation, receive any kind of information about their value, what was learned from their participation.

So the last slide I want to leave you with is just thoughts about that intersection between patient engagement and how it will benefit the drug development process in the long term. As I mentioned, we view it as one of the critical ways that we can disrupt this very traditional and inefficient, this highly risky and costly process, to ultimately derive a process that benefits everyone and that is ultimately the outcome of a true partnership

between the patient community, the public, and those of us who serve these individuals through our work within the research enterprise. It really starts with engaging the public and improving public literacy and understanding. Patient engagement begins with public engagement, and that prepares all of us in the event that we become a patient or a loved one who is supporting a patient through their journey.

And many of the other areas we touch on here, I think, relate to the concepts around a learning health environment, an environment that really embraces an integrated environment where clinical care and clinical research are better associated and coordinated, where the patients' experiences are customized, they're flexible, they're more intimate, and they're catered to the patients across a variety of different dimensions, the demographics, their needs. And so that is also a very important way that we need to think about engagement moving forward.

And then, again, I just want to also highlight the importance that the data will provide for us, that we collect, to really give us a chance to not only communicate back to the patient community, but to create this continuous learning process where we can better inform research moving forward and its connection to clinical care will be stronger as well.

And with that, I'll just say thank you again for the opportunity to share my perspective with you. Thank you.

(Applause.)

MR. CONWAY: Thank you, Mr. Getz. I'd like to thank the FDA, the Duke Clinical Research Institute, and Mr. Getz of CISCRP for their presentations.

And now we will have Open Committee Discussion and clarifying questions from the Committee. As a reminder, although this portion is open to public observers, public attendees may not participate except at the specific request of the Chair. Additionally, we request that all persons who are asked to speak identify themselves each time. This helps

the transcriptionist to identify the speakers.

Does anyone here on the Committee have any clarifying questions for FDA, for Duke Clinical Research, or CISCRP?

(No response.)

MR. CONWAY: If not, I'd like to go ahead and throw open the floor to the committee members. Does anyone on the Committee here have a topic that they wish to discuss in light of the initial presentations that we had? Go ahead.

MR. DUNLAP: Bennet Dunlap.

I'd like to thank our friends from Duke for talking about net present value. And don't be ashamed of that; don't hide it. I'm a former banker. I apologize for what I did to the American economy and fear it was all my fault.

(Laughter.)

MR. DUNLAP: But in the -- bean counters, that there's value in patient participation. It's not going to happen, but if we can get the bean counters on our side, they can help overcome the regulatory issues and the legal issues you were concerned about. So move that NPV slide up to the front. Thanks.

MR. CONWAY: Any other comments? Go ahead.

MR. DOWNS: Fred Downs.

I'm going to stress the point that was brought out, that the feedback to the patients participating in these clinical trials is almost zero or the percentages are a little bit higher -- 7% -- because I know myself, I've been to a number of trials, and I had no feedback. I don't know what the results are. I'm very curious about that. And so I think other patients, too, they said they weren't getting more feedback because we weren't enthusiastic, and we'll talk about it, and it will be word of mouth. If nothing else, it will spread to say if you participate in this clinical trial, you not only contribute to the future health of this country

and to your own future health, but you are also participating in something that you will learn more about in that process. So I want to stress that that's extremely important; getting feedback to the patient is real key. Thank you.

MR. CONWAY: Thanks, Mr. Downs.

Anybody else? Go ahead, Dr. Parker.

DR. PARKER: Mr. Getz reported that despite the vast amount of money that's being expended in drug development, we have the highest failure rates ever, and I kind of wanted a little bit more understanding of what he meant by that. What is the failure? And if we're spending it on this drug development, it's not benefiting anybody.

MR. GETZ: So that failure rate -- this is Ken Getz.

That failure rate is the percentage of drugs that enter clinical testing but did not receive approval. So about 1 in every 10 drugs that goes into clinical testing, this is after it's already been through discovery and preclinical, will ultimately come through with an approval at the end and will then move into the market.

DR. PARKER: Thank you.

MR. CONWAY: Anyone else with a question or comment for Dr. Getz?

MS. CORNWALL: Deborah Cornwall.

Just to clarify, what is the connection with clinical trials around the failure rate? Is it that they are failing the clinical trial, or is it that they are not getting a sufficient number of participants in the trial to be able to demonstrate efficacy and safety?

MR. GETZ: Those may be parts of it. Ultimately, it's really about not demonstrating that a particular drug was safe and effective. So if it has to do with the way the study was set up and the data that was collected was not promising, it could have something to do with the way the study was powered, so it wasn't able to attract and retain the number of patients that were ultimately needed. But it's all of the above.

MS. CORNWALL: And the other piece of my question, and it may pertain not only to you but to other speakers as well, is devices that pertain -- devices and drugs that pertain to the pediatric population. And I understand that pediatric participation tends to be low but also that there tend to be fewer trials available for them.

MR. GETZ: Yes, that is the case, and certainly that's the case as well within the drug development community, drug development enterprise. It has improved a lot, we see a lot more studies today, and there are some pediatric populations where there is a tremendous commitment to participate in studies so it's not difficult to enroll for them. We see very wide variation in the recruitment and retention rates in the studies.

MS. CORNWALL: But clearly different recruitment and retention issues around children?

MR. GETZ: Yes.

MS. CORNWALL: Thank you.

MR. GETZ: Yeah.

MR. CONWAY: Dr. Blackburne, and then we'll go to --

DR. BLACKBURNE: Thank you. And this is for you, Mr. Getz.

I work across a lot of different types of trial sponsors, drugs and devices. And I work on a lot of clinical development plans, and even at that point it's clear that the patient perspective isn't involved, and we bring up the protocol considerations, inclusion/exclusion criteria. How do we best message the need for that involvement because, I mean, I really appreciated your data around, you know, the impact of design, protocol design complexity being a barrier, and we spend a lot of time on that. So how do we kind of move that needle?

MR. GETZ: Yeah, that's probably one of the most important questions we have to ask when we think about the industry, and I think the comments about NPV and

demonstrating value, there has to be really a financial return on engagement, and we've demonstrated that. As Bray was mentioning, we've done some studies to show it. There are cultural barriers, as you know, and we alluded to those, this high risk aversion that -- and this sense of risk that is spread across very, very fragmented and large companies, as you know, where you have different siloed functions that often don't interact very well with each other. I would say, from our experience, every single pharmaceutical and biotechnology company wants to embrace patient engagement.

DR. BLACKBURNE: I agree.

MR. GETZ: But often, it's being championed in only one small area in a company, and it's been very hard.

DR. BLACKBURNE: It's not usually R&D.

MR. GETZ: Right. That's right. In fact, the commercial side is perhaps farther along, but there is very little communication between the commercial and R&D side. So I think part of the answer to your question is figuring out ways to communicate more broadly, perhaps through other stakeholders like this Committee, the importance of certain engagement initiatives and what we would like to see in terms of support from other stakeholders.

DR. BLACKBURNE: Thank you.

MR. CONWAY: Thanks, Doctor.

We're going to go to Amye, and then we'll be right with you, Dr. Seelman.

MS. LEONG: Very good. Thank you. Amye Leong. Thank you to our speakers.

I think, by listening to the three of you thus far, it may seem that the rest of the world is believing what we believe. But we all know for a fact that is not the case. I think about in the early days of Patient-Centered Outcomes Research Institute and how we were all shocked that someone dared to put money at the end of the period, that said if you want

to play with us, this is what you will have to do. And I have been through international and national consortia of similar kind of ilk, where people will say this should be done, that should be done, a variety of different really good, as your suggestions, Ken -- if I may call you Ken.

MR. GETZ: Sure.

MS. LEONG: You have suggested for the future. And I'm sure that all three of the organizations, of course, including the FDA/CDRH, can get together on this. But until we actually look at what motivates a clinical trial to move forward, for a clinician to get the grant, for an industry to move forward according to regulatory, political, patient-centered environment, we each are going to do our little bit to whack away at this, and I'm not sure, quite frankly, as a patient, that's good enough for me. So I would encourage each of our organizations to be a part of that solution, to join us. And, you know, I've actually had someone say, well, the FDA, in one fell swoop, could make -- by a regulatory edict, could change everything for us and could put us on the right track. I'm not sure that's appropriate methodology as well, but it certainly should be on the table.

So I would love to hear from each of you, actually, what you think are the top two things that could be done given the environment we are in today, given the trend, the science and the environment of engagement that all of us have been chiseling away at, but collectively we could make a much bigger chisel. Your ideas, please.

MR. GETZ: And I should invite my colleagues up and put you on the spot as well.

(Laughter.)

MR. GETZ: So I alluded to one of the key areas, and that is that I absolutely think that we need more regulatory and policy clarity. I think industry is sort of waiting for that.

MS. LEONG: Yeah.

MR. GETZ: And so I think that's really important. The other area that I touched on is

really the -- us thinking even more broadly about the continuum and engaging the public in this process as well, that it's not just about engaging an individual when they move into the research enterprise as a potential study volunteer or partner, but that we begin to treat clinical research as a critical subspecialty within clinical care and we begin to engage the broader healthcare community in this as well.

MR. CONWAY: Thank you.

MS. LEONG: Thank you.

MS. PATRICK-LAKE: Hi. So I really think that FDA could ask the regulatory --

MR. CONWAY: Can you just restate -- sorry, can you just restate --

MS. PATRICK-LAKE: I'm sorry. Bray Patrick-Lake.

MR. CONWAY: Yeah, restate --

MS. PATRICK-LAKE: Yes.

MR. CONWAY: -- your name for the transcriptionist.

MS. PATRICK-LAKE: Bray Patrick-Lake.

MR. CONWAY: Thanks.

MS. PATRICK-LAKE: So in the regulatory setting, when people have marketing applications, I think you ask: How did you engage patients? Was there a patient preference study? Was there a benefit-risk assessment? Where did you get this data about unmet need and outcomes of importance to patients? I think, you know, a lot of times you'll find that actually a marketing department or some type of commercial entity actually went out and gathered data, and that's really not rigorous science, an active engagement in the science of patient input. So I think, you know, there are unintended consequences when you have some type of swooping policy, but I'm actually all for it. If it were part of marketing applications, I think it would be useful.

MS. LEONG: Thank you.

DR. FARIS: So I think some of it starts with what might seem like baby steps a little bit. So, you know, the fact that we are starting to have it be the new normal to think about where does patient engagement come into the process, that we're starting to have -- you know, Jeff mentioned that everybody in our staff this year is going to engage with a patient and have that, you know, real experience. That's not everything, but it gets the conversation started, right? It gets it to be where it's a little bit more of a regular part of doing business. We're starting to see little things like our review forms that our reviewers use to look through reviews and think about the things they should be considering. A year ago we didn't have what patient engagement information was in that submission, and now we do in many cases, and those -- that isn't everything, but it gets us started driving.

So the more that we can have conversations when we're talking -- you know, we talk with sponsors all the time, and I think, to the point that was brought up earlier, I think sponsors are just as interested in this as we are, and we're all figuring out how to do it, right? And so the more we can have that be a regular part of the conversation when we're talking about what preclinical testing are you doing? Well, how does that impact the patient experience? What clinical testing are you proposing, and is this going to be practical? Is it going to get the right questions answered? How do patients feel about this?

We're going to figure this out a little bit all together, and we've done this in many other spaces, things like early feasibility studies, early studies than the first couple of patients. Ten years ago this was really new, five years ago it was still pretty new, and today it's starting to be a regular part of business, and we know how to have those conversations. I think patient engagement is at that, you know, "a few years ago" stage right now where we're just starting to get comfortable with "these conversations need to happen," and we're going to learn a lot as they happen more and more, and we'll figure out better methods for moving forward.

MR. CONWAY: I'll tell you what, we're going to Dr. Seelman. Go ahead.

DR. SEELMAN: First of all, thank you very much for your presentations.

MR. CONWAY: Dr. Seelman, can you just pull your microphone a little closer? Thanks.

DR. SEELMAN: Thank you very much for -- can you hear me?

It's on. Thank you very much for something that I remembered a long time ago that most of the concerned community and the patient community said, "Nothing for us without us." I think the FDA is going to hear about it. My question is, is there any difference in stats in terms of the experience and results of CTs for drugs and for devices? I mean, are the estimation and the basic problems the same for both, or are we going down the rabbit hole, Ken?

MR. GETZ: It's a great question, and it's one we have been trying to address. We have much more robust data on drug development than device development.

DR. SEELMAN: But you can explain -- apply that explanation to --

MR. GETZ: Why is that? In part, because the device development process has really been changing quite a bit. Initially, it was not monitored, and it was not nearly as robust. And so we also have such a wide variation in the types of devices that are developed, but it's harder to measure success in the same way we do drug therapy. However, that's starting to change, and we are looking actually to collect more of that data, and our center has been actually meeting with a number of device companies to share their data, but that's a big part of it as well. Historically, the pharmaceutical companies have shared a lot of their data.

DR. SEELMAN: So much of what you're saying, and the findings, are based mainly on drugs, and we're assuming, then, that they can be applied to the experience of CTs with devices. It's very important.

MR. GETZ: It is very important. We know that a lot of the conditions are similar, but you're right, everything that I've shared with you is really purely coming from the drug side.

DR. FARIS: So I think there is a lot of shared learning and groups like CTTI, I know, involve both the drug part of FDA and also the device part of FDA, and there's a lot of ways in which we can learn from each other. But there are ways in which devices are different, too, right? And so, you know, the kinds of issues that we run into with devices can be different. We can run into, say, mechanical failures or electrical failures that may or may not have clinical outcomes that play out in a trial but are still important, and we have to weigh them. We often have smaller trials. We often have trials that, for good reasons, can't be randomized. And so we have different and sometimes more uncertainty, and in some cases, that might be where patient involvement could be even more impactful.

MR. CONWAY: Great, thank you.

At this point, we're going to go ahead and take a 15-minute break, and we'll reconvene here at 2:42, I guess. Thank you very much.

(Off the record at 2:27 p.m.)

(On the record at 2:42 p.m.)

MR. CONWAY: Again, we'll give you an additional 60 seconds. One of the things I'd like to ask is the people at the back of the room, if you could move forward to populate the tables up near the front, that would be helpful to us for the next session in the afternoon. So while folks are getting their seats, we'll go ahead and proceed here.

We're moving forward and proceeding with the Open Public Hearing portion of the meeting. Public attendees are given an opportunity to address the Committee to present data, information, or views relevant to the meeting agenda. Ms. Williams will read the Open Public Hearing disclosure process statement at this point.

MS. WILLIAMS: Thank you.

Both the Food and Drug Administration and the public believe in a transparent process for information gathering and decision making. To ensure such transparency at the Open Public Hearing session of the Advisory Committee meeting, FDA believes that it is important to understand the context of an individual's presentation. For this reason, FDA encourages you, the Open Public Hearing speaker, at the beginning of your written or oral statement, to advise the Committee of any financial relationship that you may have with any company or group that may be affected by the topic of this meeting. For example, this financial information may include a company's or a group's payment of your travel, lodging or other expenses in connection with your attendance at the meeting. Likewise, FDA encourages you, at the beginning of your statement, to advise the Committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

FDA has received three requests to speak prior to the final date published in the *Federal Register*. The speakers will be given 5 minutes to speak. We ask that all individuals speak clearly to allow the transcriptionist to provide an accurate transcription of the proceedings of this meeting.

Mr. Conway.

MR. CONWAY: Great. You know, one more thing for folks who have entered here in the last few minutes. We're asking folks at the rear tables to move forward, if you can, and populate the front tables. It will make the afternoon go a little bit easier.

We have a number of public speakers today; therefore, I'll go over the process to ensure a smooth transition from one speaker to the next. Sorry, folks. You will have 5 minutes for your remarks. When you begin to speak, the green light will appear. A yellow light will appear when you have 1 minute remaining. At the end of 5 minutes, a red light will appear, and your microphone will be switched off. We will begin with a video

presentation from Ms. Janet Holt. Ms. Holt is unable to attend the meeting in person.

(Off microphone comment.)

MR. CONWAY: Sure. And then after Ms. Holt, we'll hear from Mr. Michael Seres, CEO and Founder of 11 Health and Technologies Limited, and our third scheduled speaker for today, Ms. Mary Cavalieri, is unfortunately not able to attend today, but we'll look forward to hearing her testimony at a future time. And it should just be a minute here before we get the video up from Ms. Janet Holt.

(Pause.)

(Video starts.)

MS. HOLT: "My first journey to Washington to speak as an injured patient was before the Institute of Medicine. I can honestly say that I did not know what the Institute of Medicine was or even what the IOM stood for. All I knew was I'd been harmed and I was at the right place. And before I continue, I have to confess that I didn't even know what the 510(k) was. It could've been a race, for all I knew. I'm very grateful to have learned how the device was marketed through the 510(k), and I stood before this committee and explained, as a patient, what had happened to me. I was a postmarket study free of charge.

"As patients, we are also stakeholders in this arena. As a patient speaking, I'm often looked as to have been regarded as non-scientific evidence or not clinically meaningful, is full of emotion and sometimes full of tears. This one medical device I received changed everything in my life, and I often felt at times that what I had to say before the FDA really didn't matter at all.

"I have learned often we are looking at flawed evidence on devices who came through the 510(k). Sometimes data has been bent to offer the desired outcomes of these companies. I realize that the FDA pays little attention to lawsuits that swirl around them, and maybe they should. Device companies are shredding internal documents when the

courts have asked for what they knew and when they knew it. I wouldn't be in this mess today if morals had any part of the decision making within some of these companies.

"I'm going to give you just a few examples of how many devices entered the market through the 510(k) clearance only to be moved into a Class III later. Two examples would be surgical mesh with 120,000 injuries and 1,300 deaths and the Essure with 26,000 injuries and 45 deaths. And the information is courtesy of Device Events.

"How did we get here? I will not speak of the lawsuits I have no firsthand knowledge about. I will offer up surgical mesh. How can you look at clinical trials and these studies when the data has been so twisted? Since nothing seems to happen between the relationship between the FDA and the device company makers, when these companies have any reports showing the companies knew before these devices were released some patients would be seriously harmed, how can hidden data not play a part? Who holds these companies accountable?

"Coloplast is now talking about marketing, beating revenue growth, and job expansion, despite its plans to pay out hundreds of millions of dollars to resolve liability for vaginal mesh. The plan, according to Lars Rasmussen in the *Star Tribune*, stated that expansion of future of growth will come from colonoscopies and incontinence products. I quote him when he says, 'We have products in the market that have been watched after the safety update came out of the FDA,' and that means the FDA approved them. 'They have looked at our total portfolio of products and said you are good to sell them.' I'm trying not to foam at the mouth after reading that statement to you.

"You see, as a patient, I do have a financial stake concerning these devices because these devices play a huge part in the quality of life. Patients normally only speak up when great harm has been done. Should this also be considered part of the postmarket study? Patients, often injured, travel at great expense to their families to what end? The harm to

them has already been done. The only incentive an injured patient has is to stop the harm from happening to somebody else. Should this not be the goal of everyone here?

"Dr. Prasad says it feels like medicine; like in medicine, if we forget history, we're condemned to repeat the errors. But why do we repeat them? Well, it just so happens that lots of people benefit financially from committing these errors. Patient safety must be the first and most important goal of every stakeholder.

"I want innovation. I want the best technology available when I'm sick. If we don't have honest clinical trials and some liability for not doing so, we will never be able to move on to other -- at the FDA, and a problem with the device does cause a questionable injury, they must have a much faster way of removing these devices in question off the market before more people are harmed. We need to find a better way.

"As I wrap this up, I must say without changes to the 510(k) process, thousands of more people will be injured in greed and untold truths. I am awed, awed for your desire to gather patient perspectives on what is a meaningful clinical trial. I do hope, in the future, the FDA will be able to make more changes and that the FDA will evaluate real patient experiences to be as important as data on the piece of paper that they are reading. We're all in this together.

"Thank you."

(Video ends.)

MR. CONWAY: I'd like to thank Ms. Holt for her testimony and move on to Mr. Michael Seres, CEO and Founder of 11 Health and Technologies Limited.

MR. SERES: I first would like to thank the Committee and Letise Williams, Lisa, and Susan Chittooran for the opportunity to speak to you today. I speak before you as a long-term patient, a patient who has participated in clinical research, a patient who is CEO of a health technology company and medical device company that has conducted multiple, and

is continuing to conduct, multiple trials. And I finally speak to you as an executive board member of Stanford University's Medicine X program, where we built a framework for modeling healthcare that included clinical trials and resulted thus in creating a workshop at the White House last year.

I believe I am as engaged as anyone could be in patient participation and in this subject matter. However, the term "patient engagement" definitely means different things to different people. Let's be honest, most patients engage in life, not health. And I would argue that this group today, whilst brilliant, is not as unique and not truly representative of patients at large who don't engage in their healthcare. And if I may, for a few minutes today, I would just like to focus on three small areas.

As you can tell from my accent, I'm British, and with Brexit looming, I'm probably not the first Brit trying to escape here. However, whilst we are technically still part of Europe, I would like to highlight a recent study where patients were researchers and it was funded by the European Commission. It was a 3-year study, and amongst its conclusion, it set out a framework of undisputed benefits around patient engagement in clinical trials. I'd like to highlight some of those points for you today, and the first would be ensuring that the unmet user need was at the start of every trial and was front and center of every trial to gain greater clarity of what was ahead. Information exchange at all times was vital and related to better research outcomes. Utilizing the patient experience improved on better engagement. Treating patients as equal partners made study changes more easier to explain and navigate. Patients who understood the purpose of a trial were better able to challenge any preconceived misconceptions, and greater understanding between patients and researchers led to better dissemination of all results. For once, as a Brit, I can say Europe got it right, and the EU clinical trials regulations of 2018 will see mandatory greater patient involvement. I hope we can get to that stage here.

My second point is very personal. I've been a patient for over 35 years. I had Crohn's disease as a 12-year-old, intestinal failure. I became the eleventh patient to have an intestinal transplant in the United Kingdom, and I'm a two-time cancer patient. But my story is no more special than anyone else's that we've heard this morning. My personal journey led me to build a technology company to help those with long-term chronically ill conditions who live connected to medical bags, such as ostomy bags, catheter bags, IV bags. Patients like me, in other words.

And as I've built 11 Health, I've had the privilege to work closely with the FDA on the regulatory pathway, and I want to include the 510(k) pathway. The FDA has been superb. They've helped me at every step of the way. I couldn't have done it without them. And as we built the company and we got involved in clinical trials, my company and I co-designed and developed every one of those trials with the researchers. We all operate a patient-led company. Our trials at Mass General, Mayo, Cleveland Clinic, Cedar Sinai were jointly conducted. Feedback given to the patient in real time, the same way it goes to the researchers, all conducted through our technology through mobile apps on the phone.

And this leads me to my final point today. Medicine X, as I mentioned to you earlier, is a model of care, has developed a model of care called Everyone Included. At its heart, it is based around mutual respect, mutual trust, and mutual empathy. It treats and values everyone as an equal, recognizing we all have a role to play. I will never be a surgeon and operate on myself. I doubt I will ever be as clever as any of the researchers that are involved in our trials or the doctors that treat me or even the engineers that help build my technology, but I understand my unmet user need better than anyone else. I understand what outcomes I want from trials. I understand how to co-create, co-design, make decisions, and communicate every single day. Isn't that the future of clinical trials and patient participation? Not "patients included," but where everyone has a seat at the table

and every opinion is as valued as the next person. It's not just about me.

But all of this relies on trust, and let's not confuse transparency and openness with trust. Perhaps transparency has replaced trust at the moment, but building trust amongst us all is complex. It requires us all to break down barriers to equip patients to cope with the way forward. I hope that the Panel, as part of their role, can equip patients to play a more active role and participation in healthcare. As a British Secretary of State for Health once said, in building a sound bite for the National Health Service, "Nothing about us without us." It couldn't be more true today.

Thank you very much.

(Applause.)

MR. CONWAY: Thank you, Mr. Seres.

To each of our presenters today, their remarks, we appreciate your willingness to share your experiences and your perspectives with us. Your feedback today will help assure us that the needs and experiences of patients are included as a part of the FDA's deliberations or in complex issues involving the regulation of medical devices. I now pronounce the Open Public Hearing to be officially closed, and we will proceed with today's agenda.

We begin the round table portion of this meeting. You, as the members of the audience, will be asked to discuss ways that patients could be involved in the various aspects of a clinical trial for a hypothetical obesity device. The scenario to be discussed is on the paper entitled "PEAC Roundtable Scenarios & Questions" that you picked up at the registration table. The round tables will focus on questions about involving patients in the design of clinical trials, how to encourage patients' participation in trials, and the best approaches to communicating results back to trial participants once the trial has concluded. Everyone seated at the round tables will have 25 minutes to discuss the questions based on

the scenario. There are no right or wrong answers to the questions, and the FDA is interested in hearing each one of your perspectives. Let me emphasize that again. There are no right or wrong answers to the questions, and the FDA is genuinely interested in hearing each of your perspectives.

FDA staff will moderate the discussion at the tables, and an FDA representative will be taking notes. I will select FDA representatives at a few tables to present the comments generated by the table members. While the actual round table discussions will not be webcast and will not be transcribed, the summaries from the round table discussions will be webcast and transcribed. We are encouraging all patients and care partners in the audience to contribute to the discussion. FDA attendees are also welcome to listen to the discussion. If the audience is full and there are patients sitting out in the lobby, I would encourage you to do the following: If they can come in to participate, that would be great, but if there is anyone sitting in the far back, we'd ask you to, again, move up towards the front so that these tables can be used the most efficiently.

The first topic to be discussed is Scenario A: Patient Involvement in the Design of Clinical Trials. Please review and discuss the scenario that is provided at your table. Again, you'll have 25 minutes.

(Off the record at 3:00 p.m.)

(On the record at 3:26 p.m.)

MR. CONWAY: The summaries of Scenario A, Topic 1 of the round table discussion. I would now like to ask the moderator for Table 1 to summarize your table's discussion. Table 1, you're being paged, thanks.

MS. ULISNEY: Hi, I'm Karen Ulisney at the FDA, and I am a policy analyst in the Center, the Office of Device Evaluation and the Clinical Trials Program.

So I had a very interesting group here. We have combined, like many have, our

tables. We're going to talk about Scenario Number 1. Just a little bit about our group demographics. We actually have industry represented, we have a company that represents patient groups represented, a few FDA folks, and some folks from the media, so we don't really have a lot of real-life patients but a lot of representation. And certainly, some of the industry folks can speak to, and all of us, to being patients as well. So on behalf of our group, I'll talk about just a couple of key points. I don't know that we need to go through the scenario, you all have it in front of you, so the first scenario is a company that is developing a clinical trial to study a novel device intended to treat obesity.

So the first question that we went through, we spent a lot of time on 1, 2, and 3, so our group won't necessarily speak to 4 and 5. But I will tell you that, again, we're coalescing and collecting notes from everyone at all tables, so if we don't reflect the conversation that's been happening on this scenario, all the tables, just know that FDA will get all of that information. So let me tell you a little bit about what we thought.

How should Company XYZ approach recruiting patients who could contribute to the design of a clinical trial? We pretty much reiterated a lot of what was said this morning in terms of it's a great idea, and companies ought to be doing that and should be reaching out to the patient communities, what's the best method to engage. The development of companies who are -- have these patient outreach or patient engagement leaders within the company, departments, or divisions that have an individual or team that is devoted to that activity and was highly endorsed, and that's kind of a new concept that I wasn't as familiar with, but we know that it's emerging and growing, and everyone believed, at least at our table, that that was a really good idea. So getting patient input also very early on in the development process was endorsed here as well, so the earlier the better. Let's go back to -- I'm trying to collect all this information, so I apologize if I'm jumping back and forth.

The concerns that a company might have, Number 2, with involving patients in the

design of a clinical trial. This was a really interesting conversation. The inputs into patient input and some of the proprietary information around product development was a key part of our conversation, so the trust of both the patient and industry side in sharing information and trusting that not only that information is somewhat protected, but that there's also a balanced view and you're representing the correct demographic, you know, that you are reaching out to those individuals and they're the right individuals, and then when you've selected those individuals, there's a trust, a mutual trust.

I talked a little bit about, and many of you may be aware of CTTI's recommendations. We heard from Bray earlier about those. Some of the early work that CTTI did addressed these issues, so it's research you might want to go to, that talked about maybe the development of a patient agreement with either individuals or entity, whomever you're reaching out to, and establish what the ground rules are for this type of engagement. So we talked a little bit about that.

The financial cost and folding this into planning a clinical trial, that was a very interesting perspective, that you may have your individual at a company that is responsible for this or a department that's responsible for this, but there's a cost associated. So the cost could also involve not only collecting this data, but also one of the recommendations to improve getting this data was to go out to where they are. Where are our patients? Where do they exist? They're in doctors' offices, they're in hospitals, they're in patient advocacy groups, they're -- rather than building it and they will come, it's more or less how do we go out and build it by interacting and engaging in patient communities. So there is a financial cost associated with that.

Number 3, what concerns might patients have with providing input to Company XYZ about clinical trial design? Again, that was kind of an interesting conversation as well, and we had to think about the trust, again, going both ways. We heard from one of the

representatives here at the table that happens to represent patient groups across a variety of disease and disorders being treated with a variety of therapeutics, devices and drugs, and it was very interesting to hear that trust about what a company is going to do with their information seemed to be paramount, and that was revealing. I don't know that I've thought of that and maybe -- in the room may not have been top on their mind, and we've heard a lot of things that patients are concerned about this morning and not being part of in the development of clinical trials, but this was an interesting perspective. What are they going to do with it, and if I tell you how I feel, how is that information protected?

A gap in patients not really having a basic understanding of clinical trials, this was really identified as a major issue. So we talked a lot about how patients could engage and be part of outcome development or endpoints, be part of inclusion and exclusion criteria, understanding and contributing to how we can improve the informed consent process, but taking a step back and recognizing that a large majority of the population and patients don't understand the basics of clinical trials. And where could we do better there as stakeholders in the clinical trial ecosystem? Could we do better in educating and finding those resources for patients so they understand what it means to be in a clinical trial and what their responsibilities are? So some of the basic sort of 101 sobering, you know, to hear that and we do need to step back and realize it.

Finally, the patients also -- what we heard from our representative that represents patient groups is that patients often can't find clinical trials. We need to do a better job in helping link patients with trials. And one of the comments -- I've heard this also, and I heard it at the table, patients who go to ClinicalTrials.gov and have absolutely no idea how to navigate that system. In fact, they find it a system that's complicated, and they can't find themselves in that database, so you know, they lose out on being able to participate in really vital trials. That's all we have.

MR. CONWAY: Thank you very much, Table 1.

The Committee is really interested in hearing the feedback from the round tables, so I'm going to go ahead and ask for the FDA person for Table 7 to come on up and summarize as well. Thank you.

DR. BOCELL: Yes. Hi, my name is Fraser Bocell. I'm a social science analyst with CDRH, and like Table 1, my table kind of ran the gamut of people who are involved with industry, people who are involved with contract research organizations, and people who are involved with patient advocacy groups and patient representative groups.

And we kind of jumped all over the map in our discussion, and one of the things that hasn't been touched on yet that I thought was interesting is talking about bringing patients in, in this area, and bringing them in, in developing the trial protocols, and the trial itself is kind of new ground. And when you're talking about going out and doing market research, there's already a set playbook for that, and companies are very used to that, and going and seeing patients, but they're not used to the legal ramifications that might surround involving patients in other steps of the process, especially since there's not really -- there's not a well-defined playbook for this right now and that several people at the table thought it might be helpful if different stakeholders could kind of give examples or give guidelines, give -- raised that you can go about doing this. That would benefit the patients and also kind of clarify things for industry, clarify things for CDRH on how do you approach this in a manner that would be beneficial to everybody.

We also talked a little bit about, kind of, the importance of sites in the trial process and how you're going to be as adaptive as you can to kind of fit the needs of the patients. And the sites really need to be clearer on that the patient is the important person in the trial and that you're not always just involved with the patient, but you're also really involved with the caregivers as well, or with the parents or anybody else who might be

involved, so that you've got to try and work around the schedules of the patients, you've got to be adaptive, you've really got to work just overall, and basically, it's not easy and that some effort needs to be put in to make sure that you're adapting and being responsive to patient needs throughout the process.

Am I forgetting anything, anything important? I think -- yeah, oh. And then the last thing we talked about was the idea that for a lot of conditions, there's this stigma that surrounds that condition, and it can have an effect on people seeking to be a part of trials; it can have an effect on trials seeking out certain patients, seeking out certain groups of patients, and that I think all stakeholders need to be mindful of the fact that the patients aren't necessarily -- it's not just about their condition, but it's also the stigma that surrounds their condition that can affect their participation and their treatment and all aspects of this process, and so it's important to really keep that in mind going forward as well. And so I think that's a nice high-level summary of what we talked about.

MR. CONWAY: I think it was great. Thank you very much.

Now, what I'd like to do is move on to Scenario B, Topic Number 2: Patient Recruitment, Enrollment, and Retention. There will be 25 minutes for this discussion as well. Please review and discuss the scenario that's provided at your table. The time right now, I have 3:40, and so 25 minutes from now, at 4:05, we'll reconvene. Thanks.

(Off the record at 3:40 p.m.)

(On the record at 4:05 p.m.)

MR. CONWAY: Okay, folks, it's 4:05 right now, and we're going to go ahead and proceed with asking the tables to provide summaries on Topic 2. I'd like to go ahead and ask for the moderator for Table 3 to summarize your table's discussion.

MR. SKODACEK: Okay, are we ready? All right. Thank you, everyone.

So my name is Ken, and I work with FDA, and I'm working with my colleagues here,

Jim and Tosia, who are taking notes. And I think, in preparation for this event, I thought oh, it would be great to be able to summarize what was said at the table, and then I realized all the different topics that were being discussed, and trying to capture all of them in real time is incredibly challenging.

So we had just a few items that I want to focus on. So, again, this is about recruitment and retention of patients of various conditions, whether they're pediatrics, patients that are older, patients that are women, patients of various racial groups. And I think one of the things that the group talked about is any pediatric patient population is a challenge, certainly due to trying to obtain parental consent and patient consent to participate.

We also used the word "stigma" again. We used the example of obesity in teenage girls, that there's some sensitivities associated with those topics, and those sensitivities certainly limit potential enrollment.

Sometimes primary caregivers may be treating hypertension or diabetes from the personal perspective of a clinician and may not have as much interest or familiarity with the care path. So one of the people at the table mentioned that in many cases for clinical trials, you might have a small handful of physicians that are subject area specialists, that they're -- maybe they're, I think we mentioned, cardiovascular interventionalists, that they're the ones actually using the device and are familiar with the device, but they don't have really the outreach, and they don't necessarily work as closely with patients that are in the care clinics and that are working with the referral physicians, so they don't always see the patients throughout the life cycle of the patient's disease and dealing with the symptoms. And you really can't engage the patients at all unless you have the physicians involved and buying in.

Physician-investigators tend not to be surveying the large communities. There's no

feeder system in place within our healthcare system, in general, and with individual healthcare facilities, and there's a lack of connection to specific patient populations. So it's challenging enough to enroll patients in a clinical trial, and then you're trying to go a step further and enroll patients with these specific conditions, and it can be even more challenging.

There's a perception that they -- that they, the patients -- won't have access to their information or these devices and that even when they -- outside of the trial, they're in their individual communities, they might have access to these devices later. So there's an overall lack of connection to the community such that -- has the patients be hesitant to participate.

It's not always clear that clinical trials are a care option, so for a lot of patients, they're involved in their overall disease treatment and condition, and they're not thinking about clinical trials all the time, and especially, obviously, for pediatric patients that might not have awareness of clinical trials and some of the treatment options available to them.

For the obesity devices, the surgeons treating the pediatric population don't always have access to the patients that they need to enroll in the trial. Perceptions of five physicians of asking patients, so they might be a little bit nervous to ask or approach certain patients. Maybe they have some preconceived notions about whether or not these patients, maybe women, might be willing to enroll or not. Some patients or many patients say that they have never been asked or approached, so again, there's this preconceived notion that they're out there, the patients are out there, they want to participate in the trial, but they're not being involved, whether it's elderly and women representation in trials.

If you don't have a chronic condition or symptoms, you may not be referred to a clinical study, so you may have the underlying disease, but if you're not symptomatic enough or your health is good enough, you might not be referred by one physician to

another until it's too late. And there might also not be anything in the patient's record, so you don't have any documentation in their chart about the need for a referral or that they have a specific condition, so that anyone scanning through those medical records can't even find those patients or what background diseases they have. There are many different treatments for obesity; why would you be referred to a clinical trial? So patients have many different options, and clinical trials are just one of those options. Some physicians might not add to the record, again, because they don't get paid. So, again, unless they're referring them for a specific reason in the healthcare system, they don't get sent down this different healthcare path and seeing a specialist.

Many of the physicians that are working with these patients don't even know that the trials exist, again, because the principal investigators at the institutions are the specialists and they don't have the connections. Sometimes the primary care physician is more involved than the actual PI, so the primary care physician for that individual patient knows these individuals and knows what their needs are, but they don't necessarily -- aren't connected to the trials.

We have how many places has a patient been before they ended up in a clinical trial, so they might have been already being referred to various different physician/specialists, and they feel like they're being passed from person to person, so by the time they get asked to participate in a trial, they might be a little hesitant. And is your medical system sophisticated enough so that you can sort patients based on specific criteria? Again, if this not in their medical record or they can't find things on ClinicalTrials.gov, it's hard to identify the individual patients.

And one of the topics that came up that is important is education, so beyond a specific trial, but wouldn't it be interesting if healthcare facilities had an ability to sort of educate patients on the overall process for patient screening and enrollment such that they

are maybe more interested in participating after being asked? And then we talked about barriers to retention. I'll just list off a few in the essence of time. Logistics, time, a family or work commitments. Maybe you're doing so well that you get the device, you get implanted with a device, and you feel much better, and then you don't end up coming back. Or you get the device and you don't feel any better, and you decide not to come back because you want to pursue other treatment options. And in some cases, if they have an implanted device, one of the opportunities is if that device needs to be adjusted or programmed in some way that they will come back. And we really highlighted the opportunities associated with mobile health technologies, telehealth, remote follow-up, such that the patients can be followed and retained without having to return to the investigational center. And there were some comments and questions about FDA's regulation of these consumer products.

How can you communicate the window of getting the treatment versus the placebo to let them know that there is a reason for them to keep -- to stay in a trial? So someone mentioned the opportunities for crossover trials. Maybe you could randomize the control group, but you want to participate or have access to the device. You give access to all the patients; that might help keep patients in the trial. Some discussions about how CDRH and CDER interact with regards to mobile health. I should mention that there is an ongoing project with CTTI, the Clinical Trials Transformation Initiative, focused on promoting the use of mobile health technologies exactly for these specific reasons.

Are there easier ways to gather data to support endpoints? In terms of weight. Can payers cover the treatment or copayment to incentivize patients staying in the trial, and how can you do that without presenting unethical inducement of the patients? And I think the best idea was asking patients directly, at the beginning of or during the trial, what it would take to keep them in the trial and have that conversation early on versus when they've already left. And someone mentioned that there are some companies like Uber or

Lyft-type technologies that might be helping patients get to hospitals and stay in the trial.

So that's it. Thanks.

MR. CONWAY: Great. Thank you very much.

And let me just take a minute here and explain one thing. We were asked a question, I think it may have been one of the patients in the audience, but there's a really specific reason why we're having FDA staff summarize the table discussions, and in the simplest form, we're going to put it like this: The staff is there to summarize and convey the candid comments that you were making at the table. They're not there to impart their own particular viewpoint or that of the FDA. And the reason for this is the process that we go through for conflict of interest before the Committee.

And so this is how we've been able to get to the point where we are being able to have a unique format, but I wanted to eliminate any concern that somehow the candor at the table is not being given back to us accurately; it's just a workaround that we have. So, hopefully, that answers the question of folks. The FDA staff went through pretty detailed training beforehand, in my opinion, not that they need it, but this was well thought out. But again, it's a workaround to make certain that this setting and this Committee actually has the candid feedback that we're interested in for the proceedings.

With that said, let me go ahead and ask the person from FDA for Table 9 if they could summarize. Thank you.

MS. SAHA: Thanks. Hi, I'm Annie Saha, the Director of External Expertise and Partnerships at CDRH, and our table had a nice mix of actual patients, caregivers, patient group representatives, and industry trade groups, so I think we've got a nice mix, and we did cover a lot of the topics that Ken's group focused on, too. And, you know, one of the main points that we discussed was in terms of how do you actually recruit and retain patients? Let's go to the places that people trust, go to the institutions that people trust if

you're trying to recruit people, so go to the churches, go to the nonprofits, use the local affiliates of the nonprofits, you know, go to social clubs, go to the local clinics. Don't just try to use, you know, primary care/academic/medical centers. So that was one big theme.

The idea of games came up quite a bit in our group, both for pediatrics but then also for even adults, that everyone likes games, so apparently that's a way to sort of keep people engaged into the trial itself. One additional comment that had come up from our group in terms of the pediatric recruitment and retention, especially for a 2-year follow-up, is the parent having to be an enforcer for 2 years, and especially if you're talking about teenagers, that's potentially a really difficult challenge for getting your teenager to keep going to follow-ups for 2 years and the parent having to enforce that and how well that would really go. So that was a big concern that we had discussed quite a bit in terms of the frequent follow-ups over the 2 years and what could be done to potentially mitigate that.

So similar thoughts came up in terms of telehealth, mHealth, and those kinds of things, but then also barriers to that is folks who may have limited cell phone access; you only have a certain number of minutes on your phone, certain number of bandwidth or gigabytes, so are you going to use that to communicate with your doctor, or are you going to use it to text people on WhatsApp? You know, there are tradeoffs that people especially are going to be taking, and we need to take that into account. So if we are trying to minimize the follow-ups or come up with different methods, we have to ensure that it's actually going to work for folks.

The idea of, especially in certain communities, the idea of distrust of the medical system certainly came up, and again, sort of going back to that, going to institutions you trust, so partnering with, you know, different centers like HPC, for example, in the African American community, groups like Howard University, etc., different types of community centers and community practitioners to really be able to try to break down some of that

distrust and be able to recruit and retain people who come from racial or ethnic areas, populations. Another thought to try to help would also include providing translation services, whether in Spanish, other languages, etc., to be able to ensure patient access and that people are going to stay enrolled and stay a part of the clinical trial. Also, incentives for being involved and how to keep people, so maybe the idea of rather than one incentive at the very end of the clinical trial, doing something more in between, like an Amazon or a Starbucks gift card for every follow-up visit or something along those lines, so incremental types of incentives over time. But also with that, there's the caveat of making sure that you're sort of treating people equally and how to handle that in your IRB protocols and figuring that piece out.

And one more highlight that I starred from our notes was ultimately treating the patients and the families with respect and treating them well. If you have the study staff working with the patients and their families and they treat them well, that's going to go a huge way. Someone at the table had discussed there was a study that was being done in the South, and the recruitment and the study coordinator was somebody from Boston, and they spoke way too fast, like probably me, you know. Even though they thought they were being courteous, it wasn't translating to the folks in the South, so understanding those kinds of just seemingly innocuous types of things and recognizing that really does -- that little really does go a long way and so -- and also sort of ensuring that you're -- a lot of people do clinical trials for the altruism. They may not benefit them personally, but it could in the future, so it's sort of appealing to that and working towards that.

We also had some discussion similarly about, you know, the study design and could you have people -- you know, if they're already seeing weight loss right away, it might just be done with it, or if they're not seeing weight loss, they may be done with the study, so you know, what do we do with that? Certainly, a couple of things related to certain gender

considerations, since a lot of times primarily women are the caregiver, so dealing with childcare to be able to go to those follow-ups. Also whether or not, depending on the age groups for females, looking at whether or not pregnancy would be an inclusion or an exclusion criterion and how that would affect people wanting to be a part of the clinical trial or even being part of the recruitment and retention. There was discussion about, you know, whether or not the follow-ups could be less painful depending on what we don't know, obviously, the follow-up visits would actually require. But if it's something that's thought, you know, painful, if you're talking about blood draws or different things like that, that might deter people, so what are different ways to ensure that it's not difficult for people to keep going into. Cost came up quite a bit in terms of clinical trials in terms of travel, transportation, a lot of things that we've heard about in the previous discussions.

And then the last point that I'll sort of talk about in terms of some way of -- in terms of communicating during the study, having people, you know, have updates, knowing what's going on with the study itself, overall, in a broader sense. But then also, you know, how people are doing overall, while still being able to maintain some, you know, patient confidentiality. And that may also help people motivate each other in knowing what's happening with the trial overall, and then it's sort of more collective reasons rather than a me, myself, and I in this clinical trial.

So I think that summarizes, Heather, pretty well?

Okay.

MR. CONWAY: Great. Thank you very much.

At this point, we're going to go ahead and take a short break, and we'll ask for folks to be back here at 4:35. Thank you.

(Off the record at 4:20 p.m.)

(On the record at 4:35 p.m.)

MR. CONWAY: Okay, it's 4:35, thereabouts, and we're going to go ahead and move on to Scenario C, Round Table Topic Number 3: Dissemination of Trial Data and Results to Participants and Other Patients. There will be 25 minutes for this discussion. Please review and discuss the scenario that's provided at your table, just like you've done for the previous two, and we'll go ahead and reconvene at 5:00. Thanks.

(Off the record at 4:35 p.m.)

(On the record at 5:00 p.m.)

MR. CONWAY: Okay, folks, it's 5:00. So we're going to go ahead and start the process again. We'll go ahead and ask for summaries of Scenario C, Topic 3, and I would ask the moderator for Table 5 to be the first to summarize your findings. So Table 5, you're on deck.

MS. WITTERS: All right, good evening. My name is Alicia Witters, and I am a CDRH employee. So interestingly enough, our group actually lost all of our patient advocacy group members right before this scenario, but luckily, we had a little bit of conversation about it in a previous scenario, so I'll try and make sure that that's reflected as part of this report-out as well.

So the question was about information sharing after our clinical trial was ended, which was unfortunately not successful. We, as a group, and even with our patient advocates did agree that yes, we should report out on the clinical trial, the data, but when is sort of situation dependent. So I'll walk you through a little bit of our conversation on that.

So we did talk about, you know, there's a certain point where we might have exhausted all options for continuing with the clinical trial in some other way, so we called that, you know, clinical trial failure. We basically exhausted all options for this type of treatment, at which point we felt like we -- a natural endpoint and we should certainly

report that out to patients in particular, particularly our patient trial participants. We talked, in previous scenarios, about ways that would make patients feel engaged, and communication, particularly about clinical trials results, was a key part of that patient engagement. So we did feel very strongly that we should report out in some way to patients, particularly those clinical trial participants, even in the case of failure. Our other scenario or our other avenue about when we might communicate about it sort of depended on whether there was an option to continue the clinical trial in maybe a different direction, in which case, you know, we may be looking at the patients who did experience successes, you know, did have significant weight loss; you know, we might want to look a little bit deeper into the possibilities to continue a trial with those patients or, you know, some modalities around them.

And then, you know, we probably don't want to report out immediately because we do want to continue on that investigatory path. We may be communicating periodically with patients about the status, letting them know the trial will continue, but we probably won't be doing a lot of reporting out on outcomes at that point. We got into what level of information should be shared in terms of by audience, you know. There may be different data needs depending on if our audience is purely patients. They may simply want to know this device works for this indication or it doesn't.

We said that other researchers may want, you know, more robust data; they want to know a little bit more about what exactly our findings were. Healthcare providers may also want more data to help make patient decisions with healthcare treatments or just for the sake of, you know, they want to dig into that data just a little bit more. We talked about the methods or places where we might report out the clinical trials information. We kept coming back to initially ClinicalTrials.gov seemed like that baseline where we would want to make sure regardless of whether our clinical trial was successful or met that sort of failure

criteria that we had discussed earlier, we would want to have some sort of outcome reported on ClinicalTrials.gov.

And then we got into a discussion about the return on investment for digging deeper into the health literacy aspects of certain patients and some of those other socioeconomic factors that were described in the scenario and we said, you know, we really want to try super hard to make sure that we're meeting, sort of, that 80/20 rule, so try and make our information as clear and accessible to as many people as we possibly can, but beyond that we'd really have to give some considerations to, you know, what the return on investment for going any deeper into customizing that information might be. So we had an interesting conversation about that.

And we also said, you know, we don't want to go too far in talking about, you know, failure modes in particular, or even in some cases where we may be retooling our clinical trial to go in a slightly different direction because we want to be careful about not encouraging off-label use, particularly before we haven't had a chance to explore that data or that device in a slightly different way.

So I think that about covers it. Vickie, did I get everything? Group? I'm seeing heads shaking yes.

Okay. So Vickie is wanting me to make sure that I emphasize the point that we -- we did agree that ClinicalTrials.gov is not the most accessible information but, again, sort of that baseline. We want to make sure it's included there. We're going to try and be as clear as possible, but we do recognize some limitations with the current template that is set by that website, so I think we would advocate for some changes there, if possible. All right.

MR. CONWAY: Great. Thank you very much. Now I'd ask the representative or the FDA official for Table 11 to go ahead and summarize.

MS. NGUYEN: Hi. My name is Mimi Nguyen, and I work at FDA also, External

Expertise and Partnerships.

And our group had very similar conversation to Group 5. We definitely made note of ClinicalTrials.gov, and it's not a very user-friendly experience to find that information, but it could be an area where there could be some outcomes are at a very high level that could be used, but being very cognizant that patients don't often know how to find that kind of information on there and is it going to be something that will be standardized.

So our group specifically said yes to wanting to communicate this information with the trial participants, but struggled with getting to a strong yes or no relating to sharing with the broader patient community. If there was a patient advocacy group that really helped in the recruitment and design of the trial, then, you know, clearly wanting to communicate results from this would be something we'd want -- they'd want to do based for the study and to really help build that trust and talk about -- we talked about the transparency and wanting to make sure that it didn't look like the company was trying to withhold any kind of information and wanting to make sure that, you know, going forward, that if there were other results or other trials that we want to do with this community, to make sure to continue to build that relationship going forward.

So one of the things that we kind of talked about towards the end with our group was really what are the different ways to talk to patients, and we heard some really great examples. So what a couple folks have talked about here, one example was they did a telecon with all the different study participants. The participants weren't able to really provide any discussion, but the site PI was able to kind of report out at a high level kind of what happened in the study and kind of what was going -- what would be going forward with that, and so that's kind of a nice model to make sure that information is being returned to the patient. Other folks have held actual events at the various site locations so that study participants can come and learn a little bit more what happened afterwards and

possibly meet some of the other folks. And one of the other things that we also talked about was that oftentimes during these trials, patients are probably blogging and talking greater with their overall community, so one of the things that would be encouraged for a company to do is try to kind of get ahead of the narrative of the fact that, you know, technically they didn't have a clinical significant outcome, but the patients themselves really valued that treatment and they really wanted to make sure to understand the difference between what's clinically significant versus what the patients really valued from the trial.

MR. CONWAY: Great. Thank you very much.

And I'd like to thank everybody for participating in the round table discussions and especially the audience for staying with us and the level of engagement throughout the afternoon. It's tremendous, from our perspective.

So this actually concludes the round table portion, and now what I'm going to ask is for the FDA folks that were there as the moderators to go ahead and come forward because at this point, what we would like to do is, if there are any questions from the Committee for the moderators, we're going to go ahead and put the questions to the Committee and ask for clarifications or anything like that, and then at the conclusion of that portion of it, we're going to move to an open session here of the Panel. So why don't you guys come on up here; towards the right-hand side would be helpful.

And for the committee members, some of the observations that you make over the course of hearing the feedback from the three round tables, staff is now available to pose questions to you or getting other clarifications based on what was talked about in more detail at the table. So let me start right here.

MS. CORNWALL: Hi, Debra Cornwall.

I had two questions that were triggered by Table 1, I guess it was, or Table 2, but probably related to issues that were discussed in other groups. I also want to thank you for

your engagement. It was wonderful to see the energy that was going on around these tables, and it will be enormously useful to us.

Two of the issues: One of them was I heard, as a potential obstacle or barrier, and we were discussing -- I know you thought we took the afternoon off, but we were actually listening.

(Laughter.)

MS. CORNWALL: And one of the issues that you raised was, as a barrier, a potential concern about data privacy, and we're curious to know whether you discussed is that personal data, meaning my data; is it collected data, meaning our data; or in fact, could it be something around the confidentiality, if it's a medical device that has some sort of electronic data tracking, are you talking about security of the device? I don't know whether you differentiated among those three or whether the answer is all of the above.

MS. ULISNEY: Hi. Karen Ulisney, FDA.

So is your question in the context of sharing the results?

MS. CORNWALL: No, this is related to the first conversation.

MS. ULISNEY: Okay.

MS. CORNWALL: The first scenario where you were talking about potential barriers and indicated that concern about the privacy of data was an issue, and we were trying to figure out well, is it personal, collected in the trial, or actually the data that the equipment might be generating.

MS. ULISNEY: Yeah, I'll turn to my group a little bit, but I think the context of that was actual personal privacy, so --

MS. CORNWALL: My privacy as a participant in the study?

MS. ULISNEY: Right. And I believe it was from our representative representing patient groups, right, we were talking about individuals' privacy, private information. For

example, could information be shared that would identify them either to the company, to others outside of the trial where permission wasn't given originally for them?

MS. CORNWALL: So would the data be identifiable to me personally, or would it be blind?

MS. ULISNEY: Well, we talked about that in terms of sharing information, so would that data, would your own data be available to you so that you could see, or would you have access to your own data in terms of getting results of certain tests or imaging that was done in the study? That was a concern that you would be able to get that information, but would that be shared with other people that don't have the authority or permissions in place to have that information?

MS. CORNWALL: HIPAA-related kinds of issues.

MS. ULISNEY: Yes, HIPAA-related kinds of issues. And we thought about that in the context -- we didn't think about it or we didn't discuss it in terms of a mobile device or data being gathered on a mobile device. We didn't talk about it in that context. It was more data sharing. For example, if you were using a registry or another mechanism for data gathering, maybe it would be linking your data --

MS. CORNWALL: Okay.

MS. ULISNEY: -- to some other data source and would -- who would have that information? Do I know that that's happening?

MS. CORNWALL: Okay, that's helpful. The other question that I had, and it was triggered by your group's discussion, but I believe it came up in at least one other group's presentation, had to do with educating patients or potential participants in clinical trials. And there was a lot of emphasis on responsibilities, you know; if you enter this trial, you need to do these 25 things. And the question that it triggered for me was did you talk about the educating of patients around -- or exploring with them potential benefits that

they would derive from participating in the study?

And the reason that I was raising that question, I come at this from a caregiver perspective, and caregivers and patients want to be treated like whole people, and there is a whole psychology that if we understood it better, we might be able to position the clinical trials in a way that was psychologically more comfortable to the family unit. And so I was just wondering if that issue came up and whether there was any discussion about how we train the people who are doing the recruitment around how to somehow -- I hate to use the word -- but "entice" greater participation.

MS. ULISNEY: Yes. That was talked about in the context of benefits, you know, when we -- when patients are consented to be part, we talked about that in the informed consent process, when patients are consented to be in the study, and you talk about the benefits; there's so much uncertainty around what clearly the benefits are. It's investigational. However, patients want to hear up front not only what it is that, you know, they might gain from it, but how they're going to contribute to the greater cause of treatments and therapies for their disease or disorder. So we talked about that somewhat, too, you know, what's the overall -- kind of the learning healthcare system sort of model? Did I leave anything else out in terms of that question?

And very important, up front, one of the things that really resonated, I think, in most of our conversations is that patients understand at the very beginning what their obligations are and that that's really clear. And the clinical trial team at the site, we would only encourage that they spend time doing that, a lot of time in the informed consent process and explaining the trial participation.

MS. CORNWALL: And my only concern was to make certain that it wasn't all responsibilities and that there -- that the benefits that I, as a patient or a caregiver, might derive would also be addressed.

MS. ULISNEY: Yes. And we talked about it in the context of coming frequently and being seen and have accessibility to your health -- to a healthcare provider as part of the trial participation and that also being a benefit that can be yielded.

MS. CORNWALL: Thank you.

MR. CONWAY: Great. Suz.

MS. SCHRANDT: Hi, Suz Schrandt.

I have just a couple questions also going back to the very first report-out. One question, just because of the way the scenario struck me, and so I'm interested in hearing whether this came out of the discussion, too, and I just didn't capture it. You talked about, you know, looking through how should this company engage patients. I remember clearly you saying they should do it early; they need to jump right on it. Did it come out that -- in fact, they're already a little behind, so if you look at the continuum of the life cycle, they're starting a clinical trial, and they could've started with patient input at ideation and discovery, and I wasn't sure if that had come out that they've actually already missed an opportunity to engage. Did that come out?

MS. ULISNEY: Yeah, it did. And I think probably that's when we started talking about industry investing in individuals in the company that are thinking about that all the time because something started as an idea somewhere, as early as it did, and if there is a person within the company that can think about that and be at the forefront of their mind. How do we engage this patient population that we're thinking about studying, that we think is appropriate for this device?

MS. SCHRANDT: Okay, okay. Second question from that group. You talked about, in terms of concerns of the company, the concern about sharing proprietary information, you know, kind of trusting one another enough to bring patients and sort of bestow on them this information that, in and of itself, has value, and I know you talked about the need for

bi-directionality; we need to have trust both ways. I just wonder if it came up in the conversation that the patients and what the patients offer might also have monetary value, so there's sort of a bi-directional value exchange. Did that come up?

MS. ULISNEY: Yeah, we talked about it more compensating them for --

MS. SCHRANDT: Okay.

MS. ULISNEY: -- participation in a trial and what that might look like and making sure that laws weren't broken --

MS. SCHRANDT: Right.

MS. ULISNEY: -- to be perceived as coercion and coercing them --

MS. SCHRANDT: Right.

MS. ULISNEY: -- to be in the study.

MS. SCHRANDT: Sure, okay. It's just -- I'm always struck by the idea that there's proprietary information in one direction and not the other, and I think what patients are bringing to the table can be quite valuable, however we want to define value.

MS. ULISNEY: Yeah, we did talk about that there were focus groups or patient interviews, you know, that type of setting. Patients, you know, again, they would be compensated for information, and it would be appropriately, so if they had to travel or you know, whatever the venue.

MS. SCHRANDT: Okay. And then the last question is actually on the very last group, so I'm sort of bookending here. Talking about vehicles, conduits for dissemination, I noticed that patient advocacy organizations did not come up, and I just wanted to know if maybe I had missed that. But actually, partnering with relevant PAOs to be vehicles for that dissemination, particularly to help contextualize results and make them more meaningful and usable, did that come up at all?

MS. NGUYEN: Yes, that did come up and that --

MS. SCHRANDT: Okay.

MS. NGUYEN: -- might've been an omission in my reporting out, so I apologize to my group for that and also to the Committee as well. So we did talk about making sure that patient advocacy groups did have some kind of debriefing, or there was info sharing with those groups that, you know, maybe we formed a relationship with or maybe are doing, you know, outreach to during a clinical trial or even after to share, you know, those outcomes. We talked a lot about building relationships in those communities and making sure that, you know, we were engaging with them all along the process, including if our trial fails and if it's successful, because we felt like making sure that future patients and advocacy groups are involved in recruitment later down the road, it was important to continue to engage them and build that relationship.

We also talked about making sure to engage with healthcare providers, recognizing that even if a clinical trial does, say, you know, not continue or end early, there is still a feedback loop that needs to occur with patients in the trial and their healthcare provider. It doesn't just stop; they need to know, you know, if other treatments need to be explored, or certainly they need that report out that, you know, your patient is no longer enrolled because the trial has ended.

MS. SCHRANDT: Great. Thank you so much.

MR. CONWAY: Great. Mr. Dunlap. No? You're fine?

Dr. Seelman.

DR. SEELMAN: Thank you. This is for all three groups, but it's divided.

The first two questions are more related to Groups 1 and 2. I was thinking, as a member of a clinical trial, how can we enhance the feeling of comfort in the design of the clinical trial? I mean, stigma has come up, which creates a certain fear. I mean, I myself have been nearly deaf most of my life, so I'm very familiar with some of this. So did the

design group talk at all about the relationship between design and designing something that would create trust and comfort for people?

DR. BOCELL: So this is Fraser Bocell speaking.

And one of the things that my group talked about is, and I apologize for hiding behind the post-it note, we talked a lot about community organizations and engaging with churches or other organizations that you can engage with these organizations that have already built trust in the community, that have already built trust with the patients, and kind of leverage them in addition to the healthcare practices that they're going through to try and -- we try and get that buy-in and get them more involved in the trial and engaged in the trial and continuing on with the trial.

DR. SEELMAN: Is that -- anybody else?

MS. ULISNEY: The only thing I'll add to that is we got some great ideas about communities of trust in certain -- we talked about it in terms of certain ethnicities, in certain groups where the trust is either in the family or in the church community, and we talked about having the members of these communities educate, let's say, the example we used was a breast cancer screening, that you would have a community of women, for example, that would be teaching perhaps younger women to older women about, you know, these are the risks and having -- encouraging these types of forums within the communities of trust.

DR. SEELMAN: Okay. My last -- the last group.

In terms of reportage and dissemination, just to keep the trust theme going, how can you enhance reportage in this dissemination so that you feel more comfortable with the output?

MS. SAHA: I did not report for the last group, this is Annie Saha, but something that came up from our group is actually feeding back to the design phase is that the informed

consent or the pieces of the trial when someone's -- the way the trial is designed, it should include what data and what's going to be communicated back to the patient up front, so it's very clear that when the trial does end, that patients know what they are going to get back, and so that was an important feature that came up, that it really needs to be way back at the beginning.

DR. BOCELL: So this is Fraser Bocell, and I can add to that a little bit in terms of we talked about tailoring how you're reporting the results to your audience, and there's always going to be journal articles and things like that, but also maybe creating a high-level summary for your patient organization and then maybe even tailoring that even more and making sure that you're providing information to your audience in a way that can be easily consumed by that audience that is relevant and makes sense to them. And certainly, there are going to be people who want to read that journal article, but that's not going to be the majority of your patient population.

MS. NGUYEN: This is Mimi Nguyen. I have one more thing I wanted to add. One of the things that our group also talked about was the fact that we may be having, you know, juvenile patients also engaging in this, so making sure you create the right type of materials that would be targeted towards a parent sharing this information with the child, as well as to a teenager, as well as to an adult, really tailoring kind of the message of the outcomes that came out of the trial.

MR. SKODACEK: Thank you. This is like the most popular question ever. So another thing that came up, I think, was really original from our group was that you could build something in the clinical protocol such that the study isn't over until you've communicated the results, and there's an opportunity to have an additional follow-up visit where the clinician or the research coordinator sits down with the patient, reviews the results, and answers questions, you know; it's a dialogue. It's not just something, a publication or a

journal or some summary, but it's actually a dialogue that occurs, and it allows them to feel sort of complete, get everything out of the way before the trial's --

MR. CONWAY: Great, thank you.

Amye.

MS. LEONG: Continuing on the same subject, Amye Leong.

The role of advocate organizations or community groups or patient advocate organizations is critical; I understand that, we all understand that, particularly those who are representing or work with or personally volunteer with these kinds of groups. We're really talking about systematizing engagement in a way that affects the greater number of people who can participate in the clinical trial.

My question to all of the groups, and you don't all have to answer this question, but I'd love to hear your ideas about because we're trying to systematize this, and granted, realizing that community groups are not in every community, that national groups are not in every community, so how you start something at ideation rather than further down the research road is an important piece. Sometimes it comes down to who do you know as opposed to what do you know, and the who do you know is all about who do they know in order to get them involved in a clinical trial.

So my question really is about how can clinical trialists and the FDA, because that's why we're here, incentivize or not but provide some sort of educational incentive, whatever that incentive might be, because we know incentives do work if established correctly; what kind of incentives might there be for our community groups who are underpaid, overworked, and everything that goes with that?

In my own field in the Arthritis Foundation in California, we cannot take on any more. We'd love to conceptually want to do more for our arthritis and bone and joint community; we get information continually about seeking representatives or seeking

individuals to participate, but we cannot keep inundating our community time and time again. So we at times, as an organization, have to protect our community and to figure out a systematic way that clinical trials education and, therefore, hopefully clinical trials participation can happen.

So I'd love to hear from any of you in either groups about how to systematize this as a way that engages from the very beginning, but yet also realizes that the community groups are taxed to the max. Any ideas? And I raise this question, actually, as the result -- and I'll pinpoint one of you, Table 11, because you raised the patient advocacy groups as a great place for clinical trial recruitment, and then I realized, well, I've been in that position as chair of my area, and it just does not happen in the way that conceptually we're talking. So I would love your ideas on that.

MS. NGUYEN: Sure. Actually, this is kind of related to some of the discussions our table had. We understand, you know, the patient community can be very taxed, but to really have patient champions that can really go out and talk to industry and help with the recruitment aspects of it after they help provide input in clinical trial and really try to create that almost broader outreach than just what one clinical site can do and really making sure that they have the right type of information they can then share with those who are interested in getting involved and also investing in various technologies; that if they're unable to come to various sites, instead of having very frequent visits, investing a hundred dollars and a digital scale that can then be read out on a regular basis that would then be shared with the trial site.

MS. LEONG: Interesting, thank you.

Anyone else?

MS. SAHA: You know, we didn't discuss it specifically in our group, but one thing we did talk about is sort of the port of entry of a patient to their disease or disorder, and that

typically is the physician. It's typically the news is coming from the practitioner or someone they know in most cases and trust, so that's the person that would be conveying the information about their disease and managing it long term. So how do we connect that physician to the resources available, the clinical trials that might be available; are they candidates for a clinical trial, for example?

One thing that we have seen that I can speak a little bit to at FDA is the emergence of, you know, registries, large registries, and physician groups who are participating in these really large registries, collecting data on a particular disease or disorder and the devices that may be used to treat that. Within these organizations, some are professional organizations that represent a particular, you know, surgical area or you know, GYN or whatever, whatever the specialty is, have become very interested in hearing the patient voice and are very interested in collecting data in these registries directly from patients.

So I think the sensitization of physicians becoming more aware of how important that voice is and then the networking within that community to know what is happening, industry is part of that. I think the more we encourage that type of dialogue, bringing all of these stakeholders together and highlighting the fact that the real port of entry, again, is the relationship between the patient and their clinician.

MS. LEONG: Thank you.

MS. ULISNEY: Just one thing to add that came up in our group is more of being able to develop that toolkit, what are the success stories of how has it worked for patient groups and also what hasn't worked. So, you know, you just said there have been circumstances where it hasn't worked, so you know, why was that, and if we know, we understand that so we don't go reinventing wheels and we see what does work and what doesn't work, and that could be an area to focus on.

MS. SAHA: Oh, and I'm Annie Saha, and that was Karen Ulisney.

MR. CONWAY: Dr. Blackburne, would you like to ask the last question on this round?

DR. BLACKBURNE: Sure, and thank you.

This came up in, I know, in Group 1 and Group 2 and sort of in Group 3, but around the lack of basic understanding about clinical trials. And I assume, on the patient part, but what I've also seen is there is a lack of understanding about clinical trials in the physician community outside of the core group of, kind of, the key PIs. Community physicians that are doing the everyday work of seeing patients don't understand clinical trials any more than patients and maybe even less than patients.

Do you have any suggestions or did it come up in your discussions of how we can improve the basic understanding? Should it be absent or away from disease, maybe general education about clinical trials, or does it resonate better when it's disease specific or both?

MS. ULISNEY: This is Karen Ulisney.

This is certainly not a problem unique to FDA, and this has been an issue identified particularly at NIH. We spent a lot of energy and resources, and we talked a little bit about that, what could be done moving forward. I think a group of experts bringing everyone together, that did happen in the CTTI forum, the C-T-T-I.

DR. BLACKBURNE: Yeah.

MS. ULISNEY: So there are recommendations for how to train the public on participation in clinical trials. Much of it is beginning to look at this becoming part of the routine clinical care, that that comes up in conversation. And I think what we did talk about is having -- when we talk about responsibility, the patient holding the clinician responsible for knowing exactly what is current in the area they're being treated for and asking those questions and asking about how would I go about finding a clinical trial. Empowering the patient, I guess, is the best way --

DR. BLACKBURNE: Right.

MS. ULISNEY: -- to kind of sum it up when we talked about what the patient could do and then direct them to the great resources that are available to educate about participating in clinical trials. There are fabulous organizations that represent the patient and provide videos and materials that help to educate about what it is to be in a clinical trial.

DR. BLACKBURNE: Thank you.

MS. SAHA: Annie Saha.

This came up in our group, is that it seems no one seems to get -- no one seems to get it. Companies don't get it right -- patients would know anything about clinical trials. Certain practitioners know more or less, but there needs to be some kind of broader system for all stakeholders to get a better understanding of what is -- you know, what are clinical trials and that that crosses really all the stakeholder communities, whether it's -- you know, the healthcare practitioners who aren't at the primary academic medical centers, patient groups, companies, everyone needs to have a better understanding of what is clinical trials and its place in clinical research and clinical practice.

MS. NGUYEN: Hi, this is Mimi. I also wanted add one more piece.

Something that came up when we discussed the first topic was, you know, we've already involved the patient or a patient group with the design of the clinical trial. Why not have them also help you develop the materials for your recruitment to also explain what the clinical trial is, as well as what are going to be the inclusion/exclusion criteria and other things? To really help the patients understand, kind of, what are they getting into when they begin the clinical trial.

DR. BLACKBURNE: Thank you.

MR. CONWAY: Great. Thank you very much.

Now what I'd like to do is ask my fellow committee members for any thoughts they

have, any ideas they want to put on the table here after listening today. We'll have a short discussion, and then after that, I'll ask Dr. Tarver if she has any concluding comments, and then we'll move to adjournment. But right now I think it would interesting, especially for folks in the audience, to see some of the discussion that we might want to have as a committee.

Go ahead, Suz.

MS. SCHRANDT: I'm afraid I'll get an after-school detention for asking a difficult question, but one thing that I've heard, and as I was actually reflecting across the day, is the distinction between patients who are purely partners and patients who are purely subjects in a clinical trial and sort of the mix in the middle, when people are doing a little bit of both. And I think back to my time at PCORI, we were very explicit about people who were partners, meaning they're not enrolled in the study; they're advisors, they're experts that are participating as a partner versus people who are enrolled in the study.

And at that time, we were making a very bright line, and I think what I'm hearing is that in the scenarios we're describing, there's a little bit more of a blend, and I guess I'm struggling just thinking about whether we need to be clear about the distinction. Is there a need to be -- I mean, certainly in academic research, the way you treat each of those buckets of people is very different. One is consented, one is not. And we were very explicit about that during my time at PCORI. So I just wonder, my other committee members or folks, if you've thought about this. Is that a distinction we always need to be making, whether we're engaging people in the trial or engaging people who are not in the trial but partners?

MR. CONWAY: Cynthia, go ahead.

MS. CHAUHAN: Cynthia Chauhan.

I have very strong feelings about that. I believe that a patient partner should be

anyone who is engaged at any level in the clinical trial process. Having been in trials myself, one of my responsibilities I see is to give feedback to the researchers on the trial and on the things they ask me to do. I think that kind of feedback from patients is invaluable. And then I think for people who have been in trials, to participate in the design and development of trials, they bring a particular expertise of the patient point of view. That is very important. So I don't see the value of the buckets. I see far more value in patient engagement regardless of where that's coming from. I don't know.

MS. SCHRANDT: A quick response. So just to be clear, I think there should be engagement of any patient who wants to be involved. I think where I struggle is if we talk about guidelines or when the FDA issues guidance or as patient advocacy organizations, if we're trying to sort of develop toolkits or frameworks or rubrics to operationalize, is it important? In response to one of the questions I raised earlier, I know we talked about providing compensation to people who are in the trial. Now, that would be different than providing compensation to someone who's a patient partner who's not in the trial; just the rules, the legalities are different depending on whether you're enrolled in the trial as a subject or serving as a patient partner.

Totally agree with what you're saying. Everyone's perspectives are important. I just wonder, as we sort of get into nuts and bolts of guidance and how to approach engagement, whether it will be important to say when you're engaging with people who are enrolled in the study subject, here's ways to do that are best practices versus when we're engaging with people who are purely partners, maybe because they have prior experience in a clinical trial but they're not currently enrolled. So that's the distinction I'm going through in my head is how do we grapple with that?

MS. CHAUHAN: I guess I see no one as a subject. I think we're all participants. We may participate at different levels. I think when we classify patient participants as subjects,

that takes away their humanity. So I feel very strongly about that obviously. So yeah, maybe you can say when you're in Trial X, you may have information that will be useful to us outside of that, but to not say because you're in Trial X you have nothing of value to offer other than being a participant in it. I'm just wanting to clarify that. I think that, as you all were talking, one of the things I was thinking about is I see this as a public health issue because it is out of clinical trials that good public health comes.

And perhaps if we took a stronger look at how can patients be the initiators of interest in trials so that they don't have to wait for a clinician or a researcher to reach out to them, because frankly, if a clinician in a community is not engaged in trials themselves, the probability of them offering a trial to a patient is extremely low. So I think part of our task is to look at how to make patients initiators of the discussion and kind of flip that relationship.

MR. CONWAY: Dr. Parker.

DR. PARKER: Monica Parker.

Because I come to this table as a primary care doctor, I'm going back to something that they said there. The primary medical relationship is with your primary care doctor or the person that you go to for whatever your problem is or is not. And it seems to me that because the primary care doctor is such an integral part of this team, that we need to do a better job of allowing the practicing clinicians to be a part of this research enterprise because many researchers who are good researchers actually go to a doctor's office to recruit patients. Why? Because there's a little level of continuity here. I have Patient A who's got congestive heart failure, and I have a cardiologist at the academic medical center who's doing congestive heart failure studies, and they are recruiting from my clinic, and I'm seeing Mrs. Chauhan, who's a congestive heart failure patient, so I know she's in a study; I can follow up better because the institution has made me aware of what complications I

need to look at. So I think that rather than operating in silos like I'm an advocate, I'm a this, I'm a that, you know, the people who are going to be real important to this game are you the patient, me the primary care person, because I have to resolve any issue you have and make sure that I call the right person to resolve a complication that may arise. So it seems kind of backwards to involve people who have no clinical entity, no clinical relationship with you in the first place.

So I think that there needs to be a stronger academic/research/industry relationship to better engage practicing clinicians so that people are not treated like they're guinea pigs or without humanity. I think you have to tie them together, and we need to do a little bit better job of that. And I think that patient engagement wouldn't be so hard if I could go to my doctor's office and get my blood draws or get my blood checks or get my x-rays locally rather than having to travel 40 or 50 miles to an academic medical center that takes a whole day to get through. I mean, why can't we do that? It would seem that it would be a little bit more easy to navigate if I'm in a convenient place.

MS. CHAUHAN: Cynthia Chauhan.

I agree. And one device that's been used very successfully is just putting posters in the doctors' offices and waiting rooms: "Ask me if there's a clinical trial that's right for you." That opens the conversation. So I think you're right, you're the connector.

MR. CONWAY: Deborah.

MS. CORNWALL: Debbie Cornwall.

One of the things that I wanted to pick up on is that advocacy, and I think this comment has actually come out both from Cynthia Chauhan but also from Dr. Parker, is that in my research, book research, for over -- with over 100 cancer caregivers, the operant question was what did you learn and what would you have done differently. And the most compelling message was I learned to advocate for myself and for my loved one who I was

caring for. And I think that, to a certain degree, we all owe it to the public to begin educating the general public about the importance not only of their relationship with their PCP, which is crucial to being able to discuss these specialist -- the more specialized kinds of issues, but also the need for them to be advocating for themselves and bringing the right kinds of questions to whether it's the PCP or the specialist that they're dealing with. Self-advocacy is a critical part of, I think, making it through today's medical system.

DR. PARKER: Being a good self-advocate requires that you have a certain amount of information to work with in the first place.

MS. CORNWALL: Absolutely. And that's a piece of what I think we need to somehow help happen. I mean, for instance, I was really struck by one of the groups that talked about the fact that there is no clear playbook. I think it was Table 7. There's no clear playbook for how this, how the clinical trial system works or should work. Well, there may be tools that could be created that would be helpful both to the PCP population, but also to the public at large that could be made available both through the PCPs' offices and perhaps through departments of public health within the community.

MR. CONWAY: Great insight.

MS. CHAUHAN: I think you bring up important points, and a point I think we need to think about is language. We're all very familiar with the term "clinical trial," and we just kind of know what it means, but if you're in the general public, I think clinical study would be much more palatable. Trial means a very different thing if you're not in this little inner world. And so we talk about patients having literacy, I think we need to talk about researchers developing literacy, too, the literacy of the patient. That is valid literacy, and it sometimes gets passed by the wayside.

MR. CONWAY: If there's one more comment or turn to -- go ahead, Amye.

MS. LEONG: I am struck -- Amye Leong.

I am struck by the quality and the quantity of great ideas that have come out from you, and I thank you for that. I, in some ways -- and maybe it's that little "wait until the shoe drops" side of me that I'm sure resides in all of us, that we might be expecting some real negativity things; we try this, we try that, it didn't work, whatever.

But I'm particularly struck by, given the amount and type of representation that we have in this public body, that the number of quality ideas and the depth of the discussion that then produced in short form -- thank you very much, FDA staff -- to let us know, in a very positive way, some of the ideas that you all have discussed. I'm really struck by the "we are all in this together" point of view, no matter what perspective you're taking. What I didn't hear is it doesn't work, none of it works. You know, maybe there's still time for someone to say so.

(Laughter.)

MS. LEONG: I think you would be outnumbered in this room. But I'm really struck by that, and I want to compliment each of you for that. This is a new process, but when you talk to the Patient Engagement Advisory Committee, we are going to engage. We are going to engage you, and we appreciate that. It was a big question mark in some ways, but we knew that hopefully only good things could come of it, and I think that once we see transcripts and get down to summaries, we'll have a much better idea of that richness, so I thank you. Thank you.

MR. CONWAY: I think we'll all echo your comments 100 percent.

At this point, I'd like to ask the FDA officials at the table in this room with you, Dr. Tarver, for any concluding comments at the end of the day.

DR. TARVER: So I'd just like to thank everybody for coming out and being actively involved in our round table discussions. We really did want to hear your ideas, your thoughts, and to consider that as we try to revolutionize how we look at the clinical trial

enterprise. So I want to say thank you to everyone in the audience that participated. I'd also like to thank the Committee for their very thoughtful comments, and we look forward to tomorrow.

MR. CONWAY: Great, thank you.

Letise, any last words?

MS. WILLIAMS: Thank you for coming.

MR. CONWAY: So, officially, this is the conclusion of the Patient Engagement Advisory Committee for today. We'll reconvene tomorrow at 8:00 a.m. Thanks a lot, everybody, for staying with us for the day.

(Whereupon, at 5:54 p.m., the meeting was continued, to resume the next day, Thursday, October 12, 2017, at 8:00 a.m.)

C E R T I F I C A T E

This is to certify that the attached proceedings in the matter of:

PATIENT ENGAGEMENT ADVISORY COMMITTEE

October 11, 2017

Gaithersburg, Maryland

were held as herein appears, and that this is the original transcription thereof for the files of the Food and Drug Administration, Center for Devices and Radiological Health, Medical Devices Advisory Committee.

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Official Reporter