FDA - Roadmap for Engaging with CDER
Public Workshop

May 12, 2017

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FOOD AND DRUG ADMINISTRATION

Roadmap for Engaging with the
Center for Drug Evaluation and Research

Public Workshop

Friday, May 12, 2017
9:10 a.m. to 2:55 p.m.

FDA White Oak Campus
10903 New Hampshire Avenue, Building 31
Silver Spring, Maryland

C O N T E N T S

C O N T E N T S (continued)

C O N T E N T S (continued)

P R O C E E D I N G S

(9:10 a.m.)

Introductions and Opening Remarks

DR. WHYTE: Good morning, everyone. We're going to start in about a minute, so if folks can have a seat. There are still seats in the front. I know no one ever wants to sit in the front, but I promise it'll be okay if you sit in the front.

I'm John Whyte. I'm the director of Professional Affairs and Stakeholder Engagement here at the Center for Drugs at the Food and Drug Administration, so welcome.

Just so you know, there is a race going on later today, the White Oak Classic, so you're kind of trapped here because, soon, certain roads will be closed. I'm joking. You will be able to get out. But everything will be so interesting, you will want to stay.

Today is our second roadmap for engaging with the center. And it's really a desire to help folks understand how to engage with the Food and Drug Administration on issues of drugs. It can be

a very confusing place. We often talk about the FDA regulates 25 cents of every dollar. There are thousands of employees here on this campus and around the country, as well as around the world. So it can be challenging when you have a question about drug approval or drug safety. Where do you go? How do you talk to people? How do you find out who to talk to?

So today really is that desire to start a conversation. Some of you are already quite familiar with the agency and our regulatory processes, and others are very new and have some misconceptions about the FDA.

Just so you know, all of you have gotten this folder and there's a bunch of materials in here, including an organizational chart, which is just the center, just the Center for Drugs, and that can be challenging. Again, who do you talk to, and when do you talk to, and what can you talk about, and what can't you talk about?

So hopefully you're going to learn a little bit about that today. And again, this isn't meant

to be the only point in time that we're going to have engagement, but really the start of a dialogue and the start of a conversation.

As I said, there are many folks on the webcast, so if you have any questions, we want to have a very interactive discussion. Please come to the mic so the folks that are watching online can hear it as well.

We are recording today's proceedings for archival purposes, so you can always go back. So I ask as a courtesy that you silence your phones and put them on vibrate, so not to disturb your colleagues or the speakers.

The full agenda is there, and what is going to be really exciting is we are going to have a Jeopardy later today. There won't be any prizes except your bragging rights that you won FDA Jeopardy, so start thinking about your team.

So we're going to get started because we like to try to stay on time. And it's my pleasure at this point in time to introduce Dr. Doug Throckmorton, who's the deputy center director for

regulatory programs.

What we've done is we've asked everyone to give us a fun fact, try to humanize these government employees that you interact with. Dr. Throckmorton, I always thought his fun fact was that he was from Nebraska, because how many of us know people from Nebraska? He's my first Nebraskan that I've met.

But his first job was detasseling corn, which is not to be confused with shucking corn. So does anyone know what detasseling corn is? I've tried to include a picture. Essentially, it's removing the wheat-looking part of the cornstalk from the plant by hand, which is very intense work.

That's the kind of person that Doug Throckmorton is, a very intense worker here. And I have the privilege of working with Dr. Throckmorton on almost a daily basis. He has been one of the biggest supporters here at the center and at the agency in creating the group that I'm in charge of, Professional Affairs and Stakeholder Engagement.

He is a strong proponent of true dialogue

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with patients, and patient groups, and health professionals, and is always thinking of ways of how do we include patient input into our regulatory decision-making. So he truly is a champion of all of you that want to work with the center and how do we do that more effectively. Dr. Doug Throckmorton?

(Applause.)

Welcome – Douglas Throckmorton

DR. THROCKMORTON: Wow. This guy sounds pretty good. Thank you, John, very much.

I will say I agree. I am a real champion of the work that you guys are doing. I'm delighted you guys are here today. I'm delighted you guys are going to spend some time.

I hope you learn a lot and apply what you learn to forward all the work we're doing together, because I think John's right. We've got to be working together. As I'll get to, I've been at the agency long enough to see a time when that was not the understanding. And I think, under Dr. Woodcock's leadership, we've charted a much

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better course.

So I know two things about the importance of external stakeholder engagement. First, it's important for me to do my job for Dr. Woodcock, for the center to do its job for the Food and Drug Administration, and for the Food and Drug Administration to do its job to meet its mission to protect, and promote, and make available safe and effective medicines for the American public. So it is an integral part of everything we do in order for us to succeed.

Second, I know how hard it is, and that's an important aspect of what John and his team are trying to help you with here today, something I hope you're able to use in the challenges that you all face.

Let me talk about importance just a little bit. As I said, I started in 1997, started as a reviewer in cardiovascular medicine. When I started, the engagement that we had I would say extended no further than the professional societies.

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So the idea of talking to a patient advocacy group -- there were not as many patient advocacy groups available, true, but the idea of, as a culture, engaging with the patient advocacy groups was really foreign. It happened. It happened occasionally. There were strong groups out there. It was not in the DNA of what we did as a center.

I would say fast-forward to the early 2000s, when we were confronted by two things, one a recognition that we needed to reinvigorate medical products development, to make it safer, more effective, more efficient; and second, that we needed to do a better job of communicating the things that we were doing and the things that we understood.

I think, at that point, Dr. Woodcock looked around and understood that, without any question, a critical part of accomplishing those two things was a greater engagement with the outside world. That meant reaching outside of the walls of the agency, talking to the external stakeholders, understanding the needs better than we did so that we could do

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our job better than we were.

I believe that vision was exactly right. I think that vision has driven a culture change in the last 10 years-plus within the center and within the agency as well. We get it. We understand that engagement is more than just a good thing to do. It's absolutely essential.

As a part and parcel of that, we've built places in the agency, places within my center, focused on external engagement, focused on making sure that happens.

John's group is obviously one of the highlights, the central parts of the work that the center is doing. I'm glad that his group reports to me. It has made enormous strides over the years that it has been part of our organization. But there are many other groups, and I'm sure you guys have been engaging with them as well.

The Office of Strategic Programs has done incredible work on our patient-focused drug development, the meetings that I hope many of you have been able to participate in.

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OHCA, Office of Health Affairs and Community Engagement, at the agency level has been named various things over many years, but is probably the longest-lived advocacy interaction group within the agency and continues to play a really important part. I chaired a two-day meeting on opioids with external stakeholders earlier in the week, and the OHCA participation in that meeting was absolutely essential.

But there may be some groups you may not think of as engaging in external stakeholder engagement as much also. The rare diseases group, I would point out. They're in the back of the room if you wonder what the definition of a rare disease is. They have candy back there, too, so definitely worth a visit.

The pediatrics group -- and I think Lynne Yao and her group may be talking later on in the morning. These groups have always, I believe, understood the importance of advocacy and engagement in important places within the center and the agency also.

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The second piece I wanted to say is I get how hard this is. FDA, like every federal organization I've ever been in or aware of, is complex and different from every other federal agency that I've ever been aware of.

So the organization at the FDA bears little resemblance, except in very large ways, to the organization at CMS, or VA, or whatever. So trying to identify who to call, how to identify a decision-maker, the right form to submit, whatever that is, is daunting under the best of circumstances, and it's challenging, especially when you get to the federal level.

I'm delighted that you guys are going to be getting an overview of the agency. I think we have worked very hard to try to demystify the agency. Our Office of Communications has a group set up specifically to help answer those kinds of questions.

I hope you reach out to them. I should have included them in my list of advocacy groups, too, because I think their leadership clearly

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understands and has put into place ways to engage the outside community.

I hope that, as a part of that overview process, you come to understand, one, that we want to help. Our interest is in making external advocacy and engagement possible and apply it to the drug development process as quickly and as efficiently as possible.

The second thing I hope you understand is that there are things that we do that we can't always talk about. So when things come up, and there are challenges, and you're wondering whether we're listening, yes, we're listening.

If we're not always responding, ask, get clarification about whether that's something that's grounded in a misunderstanding, grounded in a need to have a conversation; or whether it's grounded in something that we're not able to talk with you as fully about, just to clear up that miscommunication so that you don't misunderstand.

We want to help, we want to engage, and we want to be part of the conversation. But

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sometimes, we're just simply not able to do that as much as we'd all like to.

With that, John, I'm going to turn this back over to you. Thank you for your kind remarks. I miss Nebraska. It's a great place. You all ought to come visit sometime. Thank you very much.

(Applause.)

DR. WHYTE: So all of you should have this little keypad because we're going to do some audience response questions, which are separate from Jeopardy. So hopefully you all have one of these. If not at your table, hold up your hand, and we'll get some to you.

Part of the goal is not just to meet myself or to meet Dr. Throckmorton, but to meet many members of our team. That's part of the goal today. So you'll meet folks, and know them, and get to dialogue with them.

So I'm going to introduce my colleague, Chris Melton. His fun fact -- I don't know if it's that fun, other than he's not a doctor, but he is an avid golfer and told me that his handicap is 10.

So I guess that is pretty good, and he has played golf on two islands.

So I don't determine people's fun fact. They tell me what it is, and I just read it. So with that, I'll turn it over to Chris Melton.

(Applause.)

Audience Response Questions

Christopher Melton

MR. MELTON: Good morning, everyone. My name is Chris Melton. I'm a health communications specialist with Professional Affairs and Stakeholder Engagement. And in my role as a health communications specialist, I like to promote a culture of two-way engagement between the Center for Drug Evaluation and Research and stakeholders such as yourselves.

Now, as I go into the audience response questions, we'll have three of those to go over, and I would ask that everyone please grab their clickers that they have handy. Also, on the Web, they'll be able to respond, but they will not be showing on the screen in here today.

So for our first question, is this your first time at an FDA meeting? Select A for yes or select B for no. And as the questions come in, we'll see them tally up.

(Audience answers.)

MR. MELTON: So it looks like we have a mix of rookies and some veterans here. We definitely want to welcome everyone for your first time here, and we look forward to your attendance throughout today.

Now, we're moving on to question number 2. How confident are you in your understanding the functions of CDER? So select A for not at all confident, or select B for somewhat confident, or C, very confident.

(Audience answers.)

MR. MELTON: We'll have the results up here on the screen. We have 60 percent somewhat, 27 not at all, and then 13 very confident.

Now, we will move on to our final question, number 3, how confident are you in your building to navigate and engage with CDER, within the FDA?

A, not at all confident; B, somewhat confident; or C, very confident?

(Audience answers.)

MR. MELTON: Then our results will be coming up. Well, thank you, everyone, for your response. And now, I would like to turn it over to Dr. Whyte.

DR. WHYTE: Thank you. So we can see we have a lot of work to do to try to educate you. And just so you know, because you might think folks at FDA are very serious, we did a dry run of this with our team, and all of the answers were not at all confident, "I don't know, this is my first-time meeting." So I should have shown those results. So we do have a lot of jokesters here.

At this point in time, we're going to have a discussion about the drug approval process at FDA. And I'm delighted that my colleague, Dr. Milena Lolic, will be presenting how does an NDA work at the FDA, because many times, patient groups, and advocacy groups, and sometimes physician groups -- most of the time, when they're interacting with us, they're upset about that there

is no drug development in something like lupus, or they're upset that they're concerned whether or not a new drug is going to be approved. Sometimes it's also drug safety issues as well. But I'm being honest. Most of the time, it's about approval.

Milena's going to walk us through how this process works and let you know what the FDA does do and what it doesn't do. So we don't do clinical trials. We don't make drugs or distribute drugs. And I will say, as the folks at the Division of Drug Information at OCOM knows, whenever people call about that they've lost a drug, it's always something of an opioid nature. It's never Lipitor or aspirin.

So we don't make drugs, and we don't send drugs to you if you lose them. So we'll learn about the new drug approval process. And Milena shared with me that she recently bought a piano, and she now is learning how to play the piano. And like many doctors, high achievers, she told me she's now going to be working on an opera soon and composing an opera.

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So that's good to know, hopefully while she still does her day job and works on drug trial snapshots, which I'll just give a pitch, also is in the back. Again, on the back table, there are a bunch of resources for you, including drug safety programs, new drug approvals, which I encourage you to look at, as well as the Drug Trial Snapshots program, which Milena leads here at the center.

(Applause.)

Presentation – Milena Lolic

DR. LOLIC: Thank you, John. We'll see about that opera stuff a little later.

Good morning, everybody. In the next 20 minutes or so, I will share with you my six years of experience in the drug approval process. It tends to look like this, a lot of paperwork coming to the desk of the reviewer. And thankful to development in electronics, we are receiving most applications electronically now. But it's still a lot of pages to be reviewed.

I will start with a brief overview of the drug development and talk about what happens when

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divisions receive NDAs, new drug applications, and what happens after the approval. There will be a two-minute fast-speed cartoon summarizing about 10 to 15 years of drug development. So let's see how will that work.

(Video played.)

DR. LOLIC: So let's simplify this. Drug development is a very long and quite uncertain process. The FDA gets involved in the drug development process sometimes at the end of the pre-IND phase with a pre-IND meeting that is about to happen, describing the future plan for drug development.

The second phase, the IND phase, is the most interactive with patients, patient advocacy groups, and the sponsor of the IND, and that is where all the clinical trials leading to hopefully NDA submission will be conducted.

Phase 4 on your right side is undetermined duration, and it will last as long as the NDA is active. Of the four phases of drug development, NDA review is the shortest, about one year,

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although that's not how it feels when you review it.

I want to clarify some confusion about the terminology that's not always easy to follow. On your left side, there are different type of designations, and on the right, the types of NDA reviews, which are determined at NDA arrival or just shortly before it. And then to make this a little more confusing, we have expedited programs marked with asterisks here.

All four represent the effort to address an unmet medical need in the treatment of a serious condition.

Being placed in one of these expedited programs means that FDA will expedite development and the review, not changing the approval standards, just streamlining the process.

Accelerated approval, which is at the bottom of this slide, is actually a path that allows for earlier approval of drugs that will, again, treat a serious medical condition and fill an unmet medical need, but this approval will be based on a

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surrogate endpoint.

The clinical trials confirming the clinical endpoint will be on the way at the time the drug is approved. This may be the shortest review, sometimes about four or four and a half months long.

This is the NDA review timeline. For standard review, it takes about one year from the arrival of the NDA to issuing the action letter. There is a shorter way of approving drugs, priority review. This one takes about eight months.

In the first month or so, the reviewers take time to make sure that the application is complete and reviewable. A majority of the time of course is spent looking at the data and reanalyzing them. Very frequently during this phase, the FDA will then direct the applicant, asking for clarification of the data or asking that they be reanalyzed in some different way.

There are also a couple of meetings scattered throughout this review process that are used to communicate with the applicant how the

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review is progressing.

Perhaps the most frequent interaction occurred in the last third of the review during labeling negotiations. These can sometimes be completed literally 5:00 to 5:00 on Friday afternoon.

This whole process is confidential. There is no public sharing of the findings or communications. So how do we actually do that? How do we review the conduct?

It is not uncommon that the NDA has 50,000 or 100,000 pages, and we look through all of them. Each discipline, clinical, statistics, chemistry, toxicology, takes its section, looks through it, and a team, which is comprised of about 3 to 5 people, will occasionally ask the company for additional information. They will analyze and look to get the same result as the company that submitted it. And they will very frequently discuss the findings among themselves and the members of the team.

There is also frequent interaction with the

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other review members because the interpretation of each group and discipline heavily relies on understanding where the whole process is going. And in the meantime, numerous consultations and interactions occur during the review at the whole FDA level.

There are multiple groups, such as patient-reported outcome groups, QT review teams, multiple groups dealing with pediatric development that need to be consulted in order for this review to be completed.

So at the end of all of this work, we actually need to answer only one question. Does the benefit of the drug outweigh its risk? Sometimes FDA does it on its own and sometimes with the help of an expert. The most transparent way of expert inclusion is the advisory committee, which happens a couple of months before the anticipated date of action.

The decision to call whether the benefit outweighs the risk relies on FDA solely. There is no requirement for FDA to accept advisory committee

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recommendation, although it happens more frequently than not.

So the answer to that question is communicated to the applicant in the action letter as the approval, or complete response, or actually non-approval. The reason for calling it complete response is because it describes the deficiencies that we've found and way to address it, should the applicant decide to come back.

One or the other answer may come during the regular review clock, or sometimes it will follow within three months of that clock, or even longer. And that happens if during the review, either FDA requests and receives a lot of new data or the applicant decides to submit. If that cannot be reviewed within the allocated time, the NDA clock will be extended.

So everybody welcomes the approval. As you can imagine this very long walk, when it's over, a new, safe and effective drug is available. When that happens, FDA actually approves everything that you may associate with the drug: its name,

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manufacturing facilities, labeling, and very shortly after the approval, the promotional materials that you will see on TV or in journals.

So what happens after the approval? There is actually just more data coming after the approval. We may ask for more data as the condition of approval. If you remember the accelerated approval that we said is pretty fast, but based on surrogate endpoints, one of the conditions of that approval is that we see the clinical data, and there is a time on that when we want to see them.

We also ask, for example, that pediatric trials be done within a certain time frame. For some companies, they may actually volunteer to do that, so we will have either a postmarketing requirement or commitment.

Sometimes, the company wants to expand the development program, so there will be new data coming for the same drug, but perhaps a new population or the new indication. And for the newly marketed drug, there is a fairly large number

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of safety data that is collected immediately following the approval and continues during the life of the NDA.

We also monitor our work on NDAs. This slide shows three last years of NDA and BLA approvals based on the type of review. As you can see, we average about 100 to 110 per year. We look at the time that we spent reviewing them. And as you can see here, again, for the last three years, we can proudly say that about half of all the approvals occur at about the eight-month mark.

[Indiscernible]? We think it is. But we also look, how do we stand in comparison to the rest of the world? And this is the comparison among regulatory agencies in approvals of new entities, the newest of the drugs. Every year, FDA was first to approve more than 50 percent of the new drugs, more than any other authority.

Now, I would like to go through publicly available information once the drug is approved. Several of the drugs will have a press release within a couple of hours of approval. In general,

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this information is available for the drugs that we anticipate will be of a great public interest.

All the FDA reviews -- and there can be thousands of pages -- are public and available on drugs at FDA. Some of the text will still be redacted because there is still proprietary information contained in our reviews.

For the last two years and for some type of the new approved drugs called new molecular entities, what we have available for public are drug trial snapshots, and they're available within 30 days of approval.

So how do you access drugs at FDA? Google it, and this is what you will see once you type in a couple of letters of the drug you are interested in. As you scroll down, you will have the list of all the reviews. Again, there can be thousands of pages, so if you want to read, pace yourself, quite a heavy read and very scientific.

A somewhat shorter and much more friendlier version to read are drug trials snapshots, and this is the first page that you will see once you Google

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drug trial snapshots. Once you scroll down, you will find the list of, at this point, 90-plus snapshots that have been published in the last two years. The database is searchable by drug name, active ingredient, and date of approval. On the right side, there is abbreviated indication, the disease for which the drug was approved. On the far right is a link to prescribing information.

The main topic in the drug trial snapshots is the demographics, is the answer to the question, who participated in clinical trials. So this is one example. As you can see, and that you will see on the first page of the approved drug, the demographics break down on race.

So in this case, you see people of five different races participated in the trial, about 70 percent of our participants were men, and about half of all participants were younger than 65 years of age.

So while this information is the key of each snapshot, you will also find in them a description of the trial design, all of the results of drug

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efficacy and safety, and observed differences in efficacy and safety among certain demographic subgroups.

I would like to close with a comparison of these three different types of information that are available about NDA approval that are sorted out based upon a couple of interesting information pieces that you may find in them. And obviously, the reviews will be the most comprehensive one, but you will notice they are missing consumer-friendly information.

Prescribing information, obviously intended for professional, will occasionally have a patient insert or a med guide that will cover some parts of consumer-friendly information. However, the snapshots, which will not be as comprehensive as the other two, which do not have, for example, the rationale for approval or the demographics of the whole development program, will definitely be consumer friendly, easy to read, and provide you with that information of who actually were the people that made the core of the database used for

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the approval of the new drugs.
I'd like to thank you, and I will welcome your feedback.
(Applause.)
DR. WHYTE: So you know, all the slides are going to be available on the website as well. So those folks that are listening online will be able to find all the slides.
Now, a couple of folks have asked me about the Wi-Fi password. I hope you're all being riveted by this and you're not trying to Google things online, but in case you need the Wi-Fi, it's the FDA public access -- no, FDA Public is the network that you would log onto, and the password is publicaccess, P-U-B-L-I-C-A-C-C-E-S-S, all lower caps, all lowercase, no spaces.
That's because I've been eating candy and now have a sugar rush. Dr. Throckmorton mentioned there's candy in the back for the Rare Disease Program, so I encourage you to get some if you need your candy fix.
So there are lots of ways to engage with the

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FDA and to engage with CDER, the Center for Drugs, and we're talking about this, that you can request meetings, you can send in e-mails, you can send in materials. And a lot of times, we'll talk about the docket. And those folks that are familiar with regulatory processes know that often when we're trying to solicit comments, a docket is open and people can send in their comments, and the comments are taken very seriously and are addressed.
So it's my pleasure at this time to introduce John Wright, not to be confused with John Whyte -- a lot of people thought I was giving this talk and I misspelled my name, but I'm not.
John is from the Division of Dockets Management in the commissioner's office, and he's going to talk about how do we rock the docket. And his fun fact is he is a woodworker and musician who enjoys building and playing his own electric bass guitar. And his son is quick to let him know what grooves and what doesn't.
That dates us a little, doesn't it? Is that Earth, Wind, and Fire, "Let's Groove Tonight"? All

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right, John Wright.
(Applause.)
Presentation – John Wright
MR. WRIGHT: Good morning. Thank you, John. And, yes, my four-year-old does have fun with things. I like to make noise sometimes, and he's quick to remind me that if it doesn't sound like PJ Masks or some other wonderful show, it's not quite as fun.
So what do we do at Dockets Management? We have taken on a role in the past many years that involves a lot of public contact. The public tries to reach the FDA in a number of ways, and Dockets Management is one of those avenues that allows people to ask us, to make regulations, change regulations, and things of that nature.
We have, let's say, about 20 people in our office. It's not a large organization. However, we handle hundreds of thousands of contacts with the public every day. Now, we work for the Office of the Commissioner. Many people are under the impression that Dockets Management works for CDER

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because CDER is very large. And don't get me wrong. We do a great deal of our work for CDER. However, we serve the entire FDA, which means we have 15,000 clients, the 20 of us or so, 15,000 internal, and external, private industry, individuals, and things of that nature.
So we're fairly busy, and we actually handle drugs to laser beams. The FDA, I believe, manages or regulates almost one-quarter of every dollar spent in the United States. So you can imagine that we touch a lot of interesting things.
Now, we have three teams that handle somewhat discrete tasks, although there is a lot of overlap. The team I'm on is the Administrative Proceedings and Management Team. Our supervisor is sitting over here, Dynna Bigby.
What we do is we process Federal Register entries, which means if the agency wishes to tell the public or industry something and they want to publish it in the Federal Register, they'll come to us. And once they've begun drafting, they'll have us open up a docket number.

That docket will then hold all of the associated documents that go with that announcement. That includes many, many, many public comments in some cases to those dockets.

Now, a petition to the government is one of those things that -- of course, those of you who recall civics know that is one of the rights of organizations and citizens, to petition their government for redress, or questions, or that sort of thing, and Dockets Management is the part of the FDA that makes that a reality.

We have certain rules and regulations, of course, that state how these petitions need to look and what you need to include in them. We are extremely responsive to individuals and industry wishing to do this.

I have spent untold hours on the phone, or via Jabber, or any other technological methods, spoken with citizens, and walked them through this process, because oftentimes, the people attempting to address our agency and our government are individual citizens. At some point, they may be

desperate. They may not have a lot of avenues. So they approach us, and we will talk them through the process and ensure that they are heard.

That's one of the key things about Dockets Management. We are extremely responsive to the public. We are not the red tape that some people complain about the government being.

We also handle comment management. Now, what that means is when there is a docket or a citizen petition opened, or a regulation that's pending, the FDA wants to have some input from the public. What do you think this regulation is going to do about your industry, your company, or your interests?

Now, occasionally, the public will comment electronically. Industry may also comment, and some of these comments can be quite extensive. For example, they include things, studies, thousands upon thousands of pages long, to a simple opinion, "I don't think this is a good idea." They can be just about anything.

When they arrive at Dockets, what we'll do

is we'll collect them and collate them, and make sure that the decision-makers have a good idea of what the public and the industry believes is important about any pending regulations or matters they're interested in.

Also, we do records, and administrative decisions, and things like that. Dockets Management, as a part of the Office of the Commissioner and under the Offices of the Executive Secretary, carries records of every administrative decision made by the agency, going way back, all the way to the 1950s.

Now, what that means is if the government has made a decision about it, it involves food or drugs, and that decision was based upon a regulation promulgated before the decision was made, it means it's likely an administrative decision. It doesn't involve a great deal of research. It just involves looking at the regulations.

If that is the case, Dockets Management has the records. We know what happened. We know how

to find it. So what will frequently happen is you may have a situation in your organization or your industry where you want to, say, make a new product. And you want to say, "FDA, have you done anything like this before? Have you made any decisions? And if so, what were they based upon?"

You can do research, and you can find out, and you can say, "Dockets Management, the FDA made this decision 30 years ago. I want everything you have," and you can put in a FOIA request or you can come and visit us, and we will get you all of those records. Very little of what we hold is restricted, so you can have just about everything that we have.

So as you see the rule of thumb here, if you see it in the Federal Register and it has a docket number, we probably have a copy. Please reach out to us if you'd like to read it. Many people come to us when it's far too late and they're frustrated. By that point, they're like, help, and so we can help. We've got the records.

You'll notice I say most records requests

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are handled very quickly. Under the FOIA Act, we have 20 days to respond. Those of you with experience getting information from the government understand that it most likely takes a lot longer than that. I'm happy to report to you that, in Dockets, it usually takes a lot less than 20 days.

Now, I did talk about citizen petitions. One of the things that is very common and that is a regular occurrence with respect to CDER, and one of the things we do at CDER, are abbreviated drug applications, over-the-counter drugs.

These things are usually decided on an administrative basis. They don't involve that you submit compounds, et cetera, et cetera to scientists to get analyzed. These decisions can be made based upon the regulations and rules at hand. And when that happens, it comes through us.

Our role is purely administrative. We are not going to get your petition and tell you, "We think this will work," or, "No. This can't possibly work." We will never do that. What we will do is we'll say, "You know, it's missing a

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piece. This is what you need to add. You need to say something about the environment," things like that. We'll tell you what has to be in the petition. In fact, in most cases, we'll tell you exactly what it needs to say.

So always, just call us if you have any questions. We will guide you through it.

These are the regulations that cover submissions to Dockets Management. These are most of them, 10.20 and 10.30. These cover general submissions as well as citizen petitions, and there are many associated regulations the more specific your submissions get. However, by the time you need to make any submission, you're encouraged just to call us, and we will tell you what applies and how to make sure you comply with it.

As I said, there are some content requirements, and I mentioned, say, for example, the economic impact on a citizen petition. Many people will look at the petition requirements and go, "Oh no. I don't know how my petition is going to impact the economy," and if you call me, I'll

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quickly tell you not to worry. All you need to do is put a sentence in there, saying, "I'll tell the Commissioner if the Commissioner asks," and then you're done. So it's not that bad. And it's important just to call us if you have any questions.

Now, we did talk about comment management, and the one thing I want to stress is that comments do take a little while to get posted. Some people will comment, and that day, that afternoon, they'll call me and they'll say, "John, I didn't see my comment on the internet. Are you censoring?" And I'll say, "No. We don't have the manpower to actually censor," and we don't. We're just a little slow.

We get 100,000 of these, and there are maybe five or six people doing this at a time, so it occasionally takes a little while. It's not a conspiracy. So please don't be afraid to comment. Every single one is read.

Help. We hear this one a lot. Where do you go if you need help? Here's the most important

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thing. Pull out your cameras, get the recording because you can have our phone number. This is not at all typical of the government. But here we are. Here's our phone number and our e-mail addresses. I encourage you to speak with us whenever you have any questions.

There is also a web address there for a SharePoint site. That site is a fantastic little snapshot of what Dockets Management does. Dynna put together that snapshot some time ago, and it has come in very, very handy. Whenever people have questions, we can just send them over there and tell them to share it.

So if you'd like, you can check out that website. If you have any problems, or questions, or comments, please don't hesitate to contact us. Those are our direct office phone numbers, and we do endeavor to get back to everybody within 24 hours or less.

Do you have any questions? I may have answers.

(No response.)

MR. WRIGHT: None? Okay. Well, Happy Friday, everybody, and it was wonderful speaking to you.

(Applause.)

Questions and Answers

DR. WHYTE: I think we're going to see if folks have any questions on the last couple speakers. And I learned a lot, John. I didn't know we use Jabber, so I'll have to look that up, as well as I could come visit you to go find comments. I'll have to figure out where you are.

But I thought the issue of making comments is something that folks that are especially new to engagement with the agency don't think about. And it's really something that you want to consider as one of the ways to interact with the agency, because as John referenced, they are read, and they are acted upon. And that's one opportunity to engage.

You want to think of numerous tools and resources that you can use to get your point across. So it really is a very, very important

tool. And many folks at the agency aren't always aware of it and understand it, so it's an important point.

I do want to remind folks that if you want lunch -- and I hope you want lunch -- we cannot provide lunch for you. But you can purchase lunch at the kiosk right outside where you registered. And you should do that during the break that we're about to take because access to the cafeteria is often restricted, so it's something to think about if you want to buy lunch. Remember, I told you there is a race going on, so there are some road closures that are starting very soon for a couple of hours.

So if folks have any questions, please come to the mic. Any questions?

While someone is coming to the mic -- or she may be going to the bathroom -- remember, we're going to play Jeopardy, and that's going to be fun. So you're going to think about teams.

I think we're going to have four teams. Is that right? I'm looking at folks. Four teams. So

there are going to be four teams, and you can pick four or five people to be on your team. So make some friends, come with new people because, after the break, we're going to want sign-up, so who are the teams going to be.

So question? Hi.

MS. SANTIAGO: Hi. I'm Kristen Santiago with the cancer support community. And I was just curious, for the drug trial snapshots, are those only for approved products? And then how is it chosen which ones are up there and how long do they stay up there for?

DR. LOLIC: Thank you for your question. As of now, drug trial snapshots are only done for new molecular entities, meaning a new molecule for the first time approved in the United States, regardless of the indication.

Once they are published, they're available until, hopefully in the near future, we expand it to perhaps adding efficacy supplements or some new data on the initial approval. But as of now, new molecular entities within 30 days of approval, and

they remain on the website to be seen.

DR. WHYTE: Question in the back?

FEMALE AUDIENCE MEMBER: I didn't hear the question.

DR. WHYTE: Sure. So the question was about the drug trial snapshots, and were they for every drug, and how long will they stay on.

Milena mentioned they're for all new molecular entities, which are new molecules. So it's not for all drugs that are approved. And it's only for drugs that are approved. It's not for any information relating to drugs that are not approved.

Once it is online -- and our goal -- and Milena has been excellent in doing this -- is, within 30 days of approval, we try to get that information online. And you can sign up to get a notification that a new one has been posted.

We really do encourage you to look at those. Dr. Woodcock has been a champion of transparency, of who's enrolled in a clinical trial, particularly based on sex, race, and age, and are there any

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differences based on that demographic information.
It's one more piece of information. It's not meant, as Milena talked about, to replace the drug label, but it is important information for patient groups as they are thinking about advocacy, safety, and efficacy, and we are very receptive to comments.
I think something you'll find that Dr. Woodcock is really trying to create at the center is to have this true two-way engagement, which is separate from communication. So historically, as Dr. Throckmorton had talked about, it's really been pushing information out. When we want you to know something, we push the information out to you.
But how do we bring information back to the center, back to our officials to understand what patients are thinking, what is clinically meaningful to patients? We're going to hear about that in a little while, but really wanted to emphasize that. And that's why we want to have a lot of dialogue today. We want you to meet folks,

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meet members of CDER, meet members of our team.
So if there are any more questions, we're happy to entertain them.
MALE AUDIENCE MEMBER: One quick question, and it's for John Wright, and it has to do with -- I just want to kind of clarify.
So if I wanted to ask for access to specific information in the Federal Register, I'm not going to necessarily just contact you and say, "Can you give me everything on drug X?" Instead, I would say, "I see this in the Federal Register. Can you give me what you have on that?"
Is that kind of how it works?
MR. WRIGHT: It depends on the drug that you're asking about. Typically, Dockets Management will have the records on every approval that is not a new drug approval. In other words, if the approval of that compound, device, drug, laser beam, is based upon the regulations and it's not novel, we will have the records.
If it's novel, it's a new drug, it's a new chemical, or something like that, then those

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records will belong at the center where it's originally approved.
The exception to that are discussions that happen in advisory committees. Different advisory committees will discuss different drugs, compounds, devices, things of that nature, and we do maintain advisory committee records and many of the materials that are submitted to the advisory committees for discussion.
In those cases, we can usually get those records or we can refer you to the people, organizations that hold them. But in pretty much every case, if we don't have it, we're going to tell you how to get it. So we're still a good resource.
MALE AUDIENCE MEMBER: Thank you.
MR. WRIGHT: You're welcome.
DR. WHYTE: Okay. Anything else? All right. It is roughly almost -- sure. Got in at the last minute. Hopefully that mic will work.
FEMALE AUDIENCE MEMBER: So I have a couple of questions representing my table --

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DR. WHYTE: A couple? Okay.
FEMALE AUDIENCE MEMBER -- so I'll try to consolidate. So four dockets, mainly, so two questions.
When you're talking about pushing information out, when a docket is created or opportunities for comments come up, is it out of your office that this happens? What are the ways that the information is pushed out? Is it just through the Federal Register?
I know we've seen it in the patient newsletter, and there's an FDA guidance documents website, but are there other avenues where we would see the information other than just going to the dockets page or to the Federal Register? That's question one.
The second question is, when there are updates, when extensions are given to comments, I know for me it's sometimes difficult to learn when those extensions have happened, and what that new date is, and where that information can be more easily accessible, and quickly, because the Federal

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Register is very slow in updating that information.
MR. WRIGHT: Thank you very much for your questions. Excellent questions. The first one, how do we let the public know things, is all of those.
Let's take CDER for example. CDER has a very good website. They have a lot of information available there. That's going to be one location. Typically, they will also have subsites for any particular programs that are happening related to a specific issue.
Now, the role of dockets in public information is very, very specific in that we manage the database that is reflected in regulations.gov. So if you go to regulations.gov to look things up, what you're seeing is the product of Dockets Management. So everything in our database is reflected on regulations.gov, and that is how most of our information gets to the public.
The Federal Register often will have information contemporaneous with us. It'll all

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happen at the same time. Oftentimes, we won't know until we get a Federal Register feed. That said, however, you can always call us and find out.
Also, if you are watching a particular approval go through the works, we are not actually going to be able to provide any information until a decision has been made or a public status has been issued. When that occurs, it will go on regulations.gov, and we will get the information after the fact.
But those are the primary avenues. We don't actually issue things like press releases out of dockets. We just make sure that the information we do put out is pretty consistent in there. I recommend that most people actually bookmark regulations.gov. When they have a docket of interest, go to regulations.gov, find it, and bookmark it because, when it does have changes, like your second question about updates, those updates, we put in regulations.gov as we get them.
We also can't tell you before that update is made until it's made. There are many, many reasons

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for this, but some of the most critical is we cannot confer competitive advantage to anybody. We wouldn't know how, and we wouldn't want to get in trouble. So we're very careful about that. We release things when they're supposed to be out. So there's not necessarily an intelligence advantage to anything we release other than older records.
Does that answer your question adequately?
FEMALE AUDIENCE MEMBER: Yes.
DR. WHYTE: I think it is a good point. And something that Dr. Woodcock wants us to think about is how do you find out about things if you're not already in the know. In many ways, we always talk about the Federal Register notice and, prior to me coming to government, I did not know what the Federal Register notice was or how it works.
So how do you even find out that there is a request for information if you're not part of that loop, so to speak? And I'd be very interested -- and I know my team would as well -- in figuring out ways how do we do that. And we've explored ways. Would we create a central

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site somewhere on CDER that might be of particular interest to patients during the time that we're allowed to do it?
So that's a fair point because as part of engagement, it's really about partnerships. And there is a recognition, especially in the center director's office, that everyone doesn't come to our website for information and that the website is very hard to navigate. That's just the reality of it.
So how do we work with partners, and who are those partners? And how do we effectively engage with them? And this is still very new to the center. So we want to hear from you. And other folks have expressed it when there are meetings. Could there be a central site for all the patient-focused drug development meetings, whether they're internal or external?
We're still trying to think through those processes, but would be very interested if you have ideas to tell us how to do that, recognizing that no one size fits all, but if we truly want to

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engage, we don't want to just preach to the choir, so to speak, to those groups that already know how to manage it well. We want to educate those folks who have a perspective, and have an opinion, and don't have a large regulatory staff, or don't have a big team that can figure all this stuff out.

So that's part of today's meeting as well, to educate us about how we're going to find out about things. So the docket is a great way to communicate. But if you don't know about it and you can't figure it out, how does that help get your voice heard? So those are things we want to hear about.

Other questions?

(No response.)

DR. WHYTE: I saw a hand. Okay. So I'll try it again.

So it is now 10:15. How about we take a 15-minute break, order lunch if you like, create your Jeopardy team, and we'll reconvene a little early, and maybe we'll get out early today. We'll reconvene at 10:30. Thank you.

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(Whereupon, at 10:14 a.m., a recess was taken.)

DR. WHYTE: We can come back in. We're going to get started. We're starting a little late, but I know people wanted to order lunch, so I encourage you to come back in. And hopefully, you've ordered lunch and you've started to think about your Jeopardy team.

Now, we're going to talk about -- the government likes to measure things. And one of the things, as we think about patient engagement and measuring what's clinically meaningful to patients, is really trying to think through, how do we measure how patients feel and function.

All of them talk about, and Dr. Woodcock does as well, that when we work with patient groups and engage with patients, we really need to understand what is clinically meaningful to patients.

We may choose a measure that is a 6-minute walk test. And you may say, "Well, you know what, Dr. Whyte? That's not important," even though

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that's objective, and that's reproducible, and there's some question about all of that, but what I'm really interested in is upper strength mobility because I want to be able to change myself. I want to be able to feed myself.

We may have a measure in migraine that it's complete resolution of headaches, and you may say, from learning, from talking to all of you that you know what? I don't have to have complete resolution of my headache, but I need to be able to get to a certain level of functioning.

That's important for us to hear as we think about changing what are those endpoints. And the only way we can effectively do that is to engage with patients and talk to patients. And that is a process that continues to iterate.

So at this point, I'm going to introduce Michelle Campbell. And her fun fact is, she completed a bucket-list item recently and saw the Northern Lights in Norway earlier this year.

So how many of you have been to Norway? How many have been to Nebraska? We have a very metro

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D.C. area I think here, but it's my pleasure to introduce Michelle.

(Applause.)

Presentation – Michelle Campbell, PhD

DR. CAMPBELL: Good morning, everyone. My name is, as John said, Michelle Campbell, and I am part of the clinical outcome assessment staff, and we are based in the Office of New Drugs.

This is the group that we look at outcome assessments that are used in clinical trials, and we also manage something called a Clinical Outcome Assessment Drug Development Tool Qualification Program.

We're a group of multidisciplinary scientists, physicians, and pharmacists that are looking at outcome assessments and really looking to see is it measuring what's important to patients and how is it, and is it appropriate to be used. And I'm going to talk to you about what we do, and how we look at measurements, and what we need today.

Here's my proof that I did go see the

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Northern Lights in Norway, and as always, our standard disclaimer statements.

We're really in this new area of patient empowerment. About two years ago in the same room, Dr. Woodcock made a statement that says that patients are their experts. They are experts on their diseases and what's important to them, and that we really need to listen to our patients, and talk to them, and let them educate us, and help us in determining what's important to them.

So this has been a real good push that we're seeing the last couple years of how we involve patients. Today, we see the increasing role of patient groups. You see vast uses of communication through social media, and we're seeing a lot of multi-stakeholder collaborations. And this could be through patient advocacy groups, with industry, with academia, or with other groups coming together, and working together, and trying to evaluate what's important to patients.

The science of patient input is a high priority for us, so we are very much interested on

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how we can capture what's important to patients.

We know that it takes a village, that patients, not only are experts, but they're not necessarily an expert in clinical trial design, or instrument developments, or another term for an instrument might be a survey.

So they may not be experts in that, but they do play a key role. So what we need to do is that we need to pull all those pieces together to form that village and help create something that will work.

Some of you may be aware of FDA's Patient-Focused Drug Development initiative. And this is where patients are able to inform us on what's important to them. What this allows -- we call it PFDD -- is a more systematic way of gathering the patient perspective.

My colleague, Pujita Vaidya, will be presenting later, and will be speaking a little bit about the patient-focused drug development, but this first was initiated under the Prescription Drug User Fee Act V. And during that time, the FDA

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said they would grant 20 meetings in various disease areas. And we can say that we actually will be having 24 by the end of this fiscal year.

You can see what's been covered, a whole range. Some of these have occurred with our other center, CBER, which is in biologics. Actually, last Friday, we had one on autism here in this room.

So why are these meetings important? First, we get to hear from patients directly. These meetings bring together various CDER stakeholders and people from the Office of New Drugs, so reviewers from prospective disease in therapeutic areas. And it really helps us learn what's important to patients.

It also helps maybe identify areas of unmet needs and gaps and helps us identify what might be some potential outcomes to explore.

There is some external interest now, and we're seeing more interest in what we're calling externally-led PFDD meetings because we know there's 300,000 diseases. We just can't hit them

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all. So there's a big push to see we can have these externally-led PFDD meetings, and I know Pujita will be highlighting this later on this afternoon, or this morning, I should say. But this is really a way for us to continue to learn about new disease areas and what's important to patients.

One highlight that comes out of our PFDD meetings held here at the agency is a report called the Voice of the Patient, and it summarizes what was spoken at these PFDD meetings.

These are really critical reports that we receive back from these meetings. We use these. So in reviewing a specific disease area and we know there's been a PFDD meeting -- I know I personally have -- we'll go back and sometimes read the reports to refresh our memories to really make sure that what we're seeing and what we're reviewing is really accurately reflecting what's important to patients. So we are utilizing these reports.

We need to be able to bridge from patient input to patient-focused clinical trial endpoints, and that's where our group comes in at the FDA to

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help with that.
We wanted to find something called clinical benefit. And what that is, it's a positively clinically meaningful effect of an intervention. So how does it positively affect how a patient feels, functions, or survives?
Survival I think we all agree that's simple to determine, but feels and functions is a little bit different. So we need to understand from our patient input how to select the appropriate clinical outcome assessment to achieve this.
What we're going to be looking at is either did we decrease maybe symptom severity in a patient, in our population -- and what we're looking for is how can we measure this clinical benefit. We want to be able to describe this in labeling terms that outcome of interest measured, and we want to make sure that this isn't misleading.
So we really want to make sure that we're accurately capturing what is important to patients, and it's really capturing what the mechanism of the

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drug is really doing.
There are four types of clinical outcome assessments that we focus on in our group. The first are probably the most common type. They're called patient-reported outcomes, and it comes directly from patients. So patients, as you were all patients, think about yourself, and you know your signs and symptoms and when you may be feeling, coming down -- just say, right now it's allergy season. If you grew up in Maryland or live in Maryland, we're all feeling this.
So we probably all know when we think, oh, is this allergies, or is this something else? We can self-report, and that is the best way if we can actually accurate self-report, a patient can.
We have clinician-reported outcomes, and this is, as they say, where we're using clinicians to report outcomes of symptoms from patients and from patient experiences, because we understand there are some diseases where patients may not be able to accurately self-report, and we need to still rely on our clinicians.

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We have observer-reported outcomes. We see this often in patients, again, who may not be able to self-report, so maybe in our pediatric populations. So we're looking at observable behaviors or symptoms that we can observe, so that a parent can see and report.
Then we have our performance outcome measures, which would be your 6-minute walk as an example. And a lot of times, people lump all of those clinical outcome assessments and just use the term PROs. But really, we are looking at four very different things.
A PRO is a measurement-based report that comes directly from the patients. These are some examples such as pain intensity, seizure episodes, asthma symptoms, rescue medication use. It's an umbrella term as I said. PROs span the gamut from simple instruments such as a single-pain assessment, what is my worst pain in the last 24 hours, to perhaps complex health-related, quality-of-life measures, or broader things.
At the FDA -- and you'll probably be hearing

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this a couple times today -- we have to uphold laws and regulations. And within these regulations and standards for assessments, like patient questionnaires, patient-reported outcomes, clinical outcome assessments, they require methods of assessments of subjects' response to what we call well-defined and reliable.
Thus, we want to describe findings from these assessments in labeling those statements that are not potentially false or misleading. So not only do we recommend drug sponsors and patient groups to engage with patients to develop these clinical outcome assessments using qualitative research -- focus group interviews, concept solicitation, one-on-one talks -- we also recommend that they perform appropriate quantitative research or statistical testing of these instruments that also helps us define and look at is this instrument well-defined and reliable.
Together, with both talking with patients through qualitative research and statistical testing through quantitative work, it tells us

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whether patients can understand and respond to the intent of these questionnaires.

That's really important because what we want to know is that not only do we understand the questions, and not only are they important to patients, but can you understand. Do the response options make sense? Do they really capture what a patient feels every day?

So this is really important because, in the end, as John mentioned, we want to know if it's meaningful. So we need to make sure that even instructions and directions on an instrument make sense, that a patient will be able to complete over the course of a clinical trial.

These instruments and questionnaires provide an estimate of what is meaningful change or meaningful improvement. That's why it's really important to get your patients involved early to determine how to interpret meaningful change in improvement in the questionnaire.

That's a key word, is how do we interpret the results from these questionnaires, and, two, is

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it meaningful? We encourage early and often communications with our industry sponsors to come and talk to us about development of clinical outcome assessments, so we can help provide guidance and advice, I should say, on what they may need and things to consider.

As always, we do have a guidance available. In 2009, the agency published a guidance on how to interpret these regulations for PRO measures and intended to provide advice for clinical benefit. Many of these principles described in this guidance also fits in those other clinical outcome assessments such as observer-reported outcomes and clinician-reported outcomes.

What this does is this provides an optimal approach for patient-reported outcome developments. But we do note that in promoting increased patient-focused drug development, we need to exert some flexibility to meet the challenges of drug development.

It's important to recognize that these recommendations contained in the guidance represent

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one approach, but other approaches may be considered. And that's why we encourage early communication with the agency to talk about that, because we do recognize in some of our disease areas and drug development areas that we do need flexibility, and one example would be in some of our rare disease areas.

So why is all of this important? Why do we care? Because what we really want is we want to go from a clinical outcome assessment to a clinical trial endpoint. Your assessment is not necessarily your endpoint, but it's going to help explain that endpoint.

So what we do is we make sure that that clinical outcome assessment is being used in the correct population of the attendant, maybe treatment population, or we call the context abuse. What group are we really studying? What is the concept of interest or what exactly are we trying to measure? Is it symptom severity? Is it frequency of events?

That's our interest. We want to make sure

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that we're capturing that correctly with our outcome assessment.

Finally, can we see a clinical benefit? Is the instrument sensitive enough to detect change? We want to make sure that we're able to see if there was improvement from a drug, that we were able to capture that correctly. And ultimately, if we have all of those in place, we can hopefully be able to form what an endpoint would be in a clinical trial.

We face a challenge. We know that PROs are important in some diseases and that PROs may be the only direct way to assess a clinical benefit. So well-developed and fit-for-purpose instruments, however, may not exist for many diseases. So in some cases, well-developed outcome assessments may exist, but PROs are needed to provide the patient perspective to understand if, say, a small change of walking ability, as measured in a clinic, really makes a difference in patients' lives every day.

I think that's really important, that we want to make sure that that change we see is

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important to patients and impacts their daily lives.

So how do we handle this challenge of not having exactly what we need, but we know we need to develop a clinical outcome assessment? This is what we call our roadmap, ironically going with our title of our workshop today. We like our roadmaps here.

But this is actually something that -- it's a lot to digest at this moment, so please don't take it all in. It is available on our website. But it's a roadmap to patient-focused outcome measurement, an approach, an optimal approach, really, and trying to develop and select an appropriate outcome assessment.

So what is really important is when you're look at this roadmap, you see three columns. What we encourage is that people start from the beginning. The first column is understanding the disease or condition. And that's when we're going to really talk to our patients, talk to our clinical experts who may help establish that.

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So during this time, we're going to understand what is the natural history of the disease; what is the population; is there subpopulations within it; is there different severity levels; do these severity levels look different among that patient population; what are current treatment options; is there a treatment option.

Then getting the caregiver, patients, clinician perspectives: what would be clinical benefit to them? What is the impact of the disease on their daily lives? So this is the opportunity through this qualitative work to have these discussions.

As we move on in this roadmap, we wanted to identify, from learning from our patients, what is really an important concept that we may be able to measure that a drug may be able to mark a clinical benefit in. So we'll determine that.

Then you want to define, again, that population you want to study, and then ultimately select what is the appropriate way to measure that.

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So is it something in pediatrics where we may have to look at something that's observable and use an observer-reported outcome, or is it something we can get direct patient response from?

Then finally we have how do we select the appropriate measure. So sometimes we may be able to go to an existing instrument and just make minor modifications, and do that, or sometimes we have to start from scratch. So this lays out ways to approach that.

We don't want this to be seen as a hurdle or barriers to instrument development and clinical outcomes assessment development, but it just really is that roadmap and maybe a framework to think about when approaching an appropriate selection of the desired outcome measure.

This is just a quick example we showed one time for idiopathic pulmonary fibrosis to just kind of show the things and ideas to consider, so understanding the disease, what does that population demographics look like starting from that first column? Is there any therapeutic

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availability for treatments? What are the key symptoms?

Then going through and just trying to find that, and just give a sense. This is just an example of one that you could use to help you in a disease area. And I think we've realized over time, as we talk about our roadmap, putting an example together of a disease kind of shows how one may be able to use them.

We know that patients' input ultimately helps us, and it helps us here at the agency. It helps us determine what to measure, what is measured to provide evidence of that clinical benefit; how best to measure the concepts in a study; and what is meaningful improvement.

Often when we are talking about instrument development and talking with our sponsors, we often say, well, what's important to patients? Go back and ask the patients. What was said in your qualitative work? We want patients to be thought about and asked early on what would be that meaningful change.

Some ways that stakeholders can work with the agency, to work with the agency and try to seek advice on clinical outcome assessments, development, and review, there are actually three pathways. The first is to that traditional IND/NDA/BLA pathway, and that is handled within those programs specifically.

The second is through our drug development, clinical outcome assessment qualification pathway. And this is outside of the individual drug development program. This is a voluntary program that is meant to work in areas of unmet need for development of clinical outcome assessments in a pre-competitive fashion.

So we're looking at development of novel instruments, perhaps. And the real goal of qualification -- and it's important to emphasize that a qualified instrument does not need to be used in an individual drug development program -- is that a qualified instrument, if an instrument is qualified, can be used in multiple drug development programs based on that specific

population and targeted area of interest that they're measuring.

So we like to say, based on its context of use or population, and based on that concept of interest or that targeted aspect we're measuring, this instrument we feel can be used and is sensitive to measure change, and we can use it in multiple drug development programs.

So this is a growing program, and we work with a variety of submitters from individual academics to large consortia. And again, this is voluntary and in the pre-competitive space.

The third way is through our critical path innovation meetings program that has occurred recently. Again, this is outside of individual drug development programs, so these meetings are really meant to be for early novel technologies, methodologies that people may want to explore.

It's a non-binding meeting, so some high-level thinking and inputs from various stakeholders within CDER. Some of our colleagues here, who you've been hearing from presenting, and from PASE,

they participate. People from the Office of New Drugs participate.

So different groups participate, and talk about, and listen to ideas that patient advocacy groups may have, other outside stakeholders may have, and just kind of get in some early thinking of this. Again, these are informal meetings, they're non-binding, and they are outside the scope of an individual drug development program.

So some just closing thoughts to think about, the FDA encourages the development and implementation of patient-focused clinical outcome assessments in clinical trials to support drug approvals and labeling claims.

As a reminder, and we cannot emphasize enough, really, early patient input is critical in the road of that development. And actually, in the areas of unmet need, if we can get early engagements and be done in a pre-competitive space early, it's also beneficial.

The identification tools is just one aspect of patient-focused drug development. The values of

patients' needs to drive the selection of these outcome assessments is remembering who the ultimate end user is, which is our patients.

We are continuing to learn best ways to engage patients in drug development. And again, we do encourage early communication, so to reach out to us and have these early discussions and helping. With that, I thank you.

(Applause.)

Questions and Answers

DR. WHYTE: Given the importance of this topic, we wanted to make sure -- because you're giving a lot of good information -- and again, the slides will be available -- if folks had any particular questions about this, Michelle has some time to answer some questions now.

So if you have a question, please come to the mic. There's one in the back, somebody that works here.

Go ahead. Can you come to the mic? See, even at FDA, we all don't know everything, so don't feel bad.

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FEMALE AUDIENCE MEMBER: I learned a lot. Thank you, Michelle.
DR. CAMPBELL: You're welcome.
FEMALE AUDIENCE MEMBER: My question was, I don't know if it's allowed, but I'm wondering if it's possible to share an example of, say, one example where the patient-reported outcome was useful in development, and why it worked out so well for the development plan, and maybe another example on how it led the whole development plan astray.
DR. CAMPBELL: I probably can't get into the second part of that question, but I can give some examples that we have actually publicly talked about where patient-reported outcomes have made it to labeling and help support a labeling claim.
One is Kybella. That did go to an advisory committee meeting. And that group worked closely with the clinical outcome assessment staff through their drug development program pathway in helping to develop what was needed to measure that endpoint of interest.

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So that is an example. And there was an AC meeting. So as we learned from Dockets Management, you can go back and actually see and learn about that. I do know that information is available because it did go to AC. But that's an example.
There's an example that's talked about in oncology a lot with the drug Jakafi, had some labeling that was used, and that's an example they use a lot in oncology because there's some challenges in oncology and the use of clinical outcome assessments, just the nature of how their trial designs are.
So those are two examples that we often hear about and can be used. So there are examples where there are successes. And I think there's probably a lot more successes than we know. And if you really think about it, a patient daily diary in essence is a patient-reported outcome, so it may not be specifically saying that it was used in a clinical outcome assessment, but one was probably used to meet what an endpoint was.
Next question?

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MS. DUFF: Hi. Thanks. My name is Jocelyn Duff. I am here from a nonprofit organization called Cure CMT4J. This is a disease. It's an ultra-rare. It affects about 22 people worldwide, and my 11-year-old daughter is affected by this. It's very much like ALS. We just had our diagnosis about a year and a half ago.
We started our foundation. We're in the very early process of this. So a lot of what we're talking about here today feels to me eons away. But I was intrigued by your comment in your slide with the critical path innovation meetings pathway and just wanting to hear you speak a little bit more about that if you could and who best to contact.
DR. CAMPBELL: Sure.
MS. DUFF: Right now, we're in preclinical trials and every day is a critical day with this disease. And so we're trying to really get all of our ducks in a row and make sure we're thinking about everything as we go forward towards a clinical trial.

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DR. CAMPBELL: Sure, not a problem. So the critical path innovation meetings are housed out of the Office of Translational Science. And actually I think you could probably Google critical path innovation meetings FDA, because I Google everything when I need to find something on the FDA site myself. But I know they have a really good website.
So what they do is they lay out what they are, and they actually have the requester to submit to have a meeting. So a person explains what they are, kind of revamps what I said, that these are usually high level and novel.
There's a request. And there's actually an e-mail address associated with that website. I feel like it's cpimrequest@fda, but don't quote me on that, but it's along the lines of that. But that is available. It's on their site.
In the form that someone who's interested would submit, you'd list information, but you talk about maybe what your questions are to the agency, want to cover, maybe a little history of the

disease, and then you submit your request.
It is my understanding that the person, the project manager for that, reaches out and contacts. And what happens when those meetings happen is that the submitter really sets that agenda of the questions you want to ask the agency and presents slides, and really does a very informal presentation of the disease or depending on what -- so if it's a disease, for example, and you have questions about trial development, having that presented.
These can be held in person or via teleconference. If they're in person, they're here on our campus here, but if not, we have groups that obviously cannot get to this area, and that we do have them via the Web.
But there is a page that is available. Like I said, Google is our friend here, and I would encourage just looking for that. But they lay out exactly what you need, and the form is pretty clear. And they do have an e-mail address, and they're very good at responding to questions and

the comments, and helping people navigate that system.
Yes?
MS. WHITING: Hi, my name is Grace Whiting. I'm with the National Alliance for Caregiving. And I wanted to know if you could touch a little bit more on observer-reported outcomes and what you view as the role of the family caregiver, whether it's a person who's a blood relative, or friend, or neighbor who's caring for someone, not just in pediatric and cognitively impaired patients, but in other populations as well.
DR. CAMPBELL: Right. For an observer-reported outcome, we want it to be something, either behaviors or symptoms, that an outside observer other than the patient can report. An example we give is -- I know you said no children, but this is an example I think we can all understand is, is my child in pain?
Pain is a really hard concept to measure, even if I was reporting it myself. So that is a really hard question if we ask an outside person to

say is this child in pain.
So that's an example of why we would say it's really hard to ask that question. What we might want to say is, are there behaviors that maybe a child makes or a person that may be associated. So that's why you want to learn these behaviors and things you can observe from the patient, so you'd be able to accurately report. So that would be a way in that development.
We do rely on our caregivers or outside people -- depending on the trial again -- it's going to be very dependent on the specific disease of interest, and the course of the disease, and who may be the best primary reporter. You may have things where you have school-aged children, and actually the teacher may be the better reporter or something like that.
So you have to really select, and that roadmap helps you determine who's actually the best reporter of those observable symptoms that someone may display. So there are areas where we definitely know that our caregivers are people who

help assist to play an important role.
It's always important, I think, having been on the other side, been in academia, so I was a researcher and having the same reporter every time. Designating who would be the primary reporter decreases some measurement error we'd be looking at to make sure we get something accurate. But we do discuss and try to identify who could be that best person, and again, it's going to be disease specific, I think.
DR. WHYTE: Maybe one quick question. Sure.
MS. WEST: Hi. I'm Melissa West. I'm with the Kidney Health Initiative, and it's a follow-up on that, which is -- and you mentioned symptoms. One in our community in particular is depression, and yet in some of our clinical settings, we have care teams who are observing, but obviously they're not the one reporting depression.
Has depression ever been considered underneath an observer-reported outcome?
DR. CAMPBELL: That's an interesting question, and let me find the best way to try to

answer your question if I can. I would say, if we're looking at depression alone, I think it often is a mix between probably patients just knowing what the symptoms are and perhaps an observer or caregiver, so it could be a combination.

So we do recognize that in some disease areas, it could be a multitude of input you're getting. So the more actual things you're getting kind of tells a better story. We have seen where you're getting multiple input available from different perspectives, not only the patient, but maybe a caregiver or clinician. Well, thank you much.

DR. WHYTE: Thank you.

So I'm delighted to introduce Mary Ghods, who is a pharmacist in PASE. And her fun fact is she is an impressionist oil painter. So I'll be looking forward to seeing those oil paintings next week. Mary is going to use those audience response questions, so you want to come up to the mic, Mary?

Audience Response Questions - Mary Ghods

MS. GHODS: Thank you, Dr. Whyte, for the

introduction. I'm still a beginner, so no requests please.

So now we have our second set of polling questions for the audience, so if you have your clickers handy, please, we'll begin. There will be four questions in this session.

Our first question is who develops and test drug and biological products before they reach the public? Is it, A, FDA; B, physicians and healthcare systems; C, pharmaceutical companies; or D, all of the above?

(Audience answers.)

MS. GHODS: I think we have it locked in, and we'll show the responses. Well, the correct answer is, C, pharmaceutical companies. So maybe we could answer some questions on that if you have any questions on that later. Thank you.

We'll move on to our second question. Among the world's preeminent regulatory organizations, which approves new drugs the fastest? Is it A, European Medicines Agency; B, is it the U.S. FDA; C, Health Canada; D, Japan's Pharmaceutical and

Medical Device Agency; or E, Australia's Therapeutic Goods Administration?

(Audience answers.)

MS. GHODS: So as a hint, it may be where you are now.

Very good, 86 percent of you got the correct answer, U.S. Food and Drug Administration. Thank you for your attention.

All right. Our third question, what initiative did the FDA launch in 2013 to gain patient perspectives on specific diseases and their treatments through a series of patient meetings to better inform the drug review process?

Is it, A, the Clear Path Initiative; B, the Safe Use Initiative; C, No Clinical Trial Left Behind Act; or D, patient-focused drug development, also known as PFDD?

(Audience answers.)

MS. GHODS: Ninety-five percent said patient-focused drug development, which is the correct answer. Very good. Thank you.

Our last question is a true-false. Generic

drugs are as safe and effective as the brand-name drugs. A, true; B, false?

(Audience answers.)

MS. GHODS: Very good, 89 percent responded with the right answer, true, generic drugs are as safe and effective as the name-brand drugs. Thank you very much for your time and attention.

(Applause.)

DR. WHYTE: I'm sure it was the Canadians here voting Health Canada as the quickest. So at this point, I'm delighted to introduce my good friend, Larry Bauer, from the Rare Diseases Program, who's going to talk about supporting rare disease drug development and CDER's Rare Diseases Program.

We can pull Larry's picture up, because this is his fun fact. He once attended a music festival in the middle of the Sahara Desert, slept in nomads' tents, rode a camel, and was bit in a foot by a scorpion as part of the experience. And it was not on a recent United Airlines flight, so that's good to hear.

(Laughter.)
DR. WHYTE: But much of our work here really is in rare diseases when we hear from patient groups, and that makes sense because it's that sense of urgency and that need. And you have a great quote back there about how we often learn in medicine that we're taught not to think about zebras, which are unusual presentations of disease. But for millions of people every year, they are a zebra, and we need to really address how we effectively engage with those patients.
So I'm waiting for Larry to come up. Maybe it's left to me. There are some links, Qs and As, and there we go. I could pretend that we got your picture on the -- but that's not.
Larry is really one of the best champions here, and then there are several members of his team as well. And I think you'll enjoy hearing what he has to say. So Larry Bauer?
(Applause.)
Presentation – Larry Bauer
MR. BAUER: Good morning, everyone. Thank

you, John, and thanks to our colleagues in PASE for inviting me to participate in the conference today.
As John mentioned, a lot of the work here at the FDA and a lot of the work you're doing is related to rare diseases. And at the break, I met several of you, and quite a few of you are already working in the rare disease space.
So I'd like to tell you a little bit today about how at the FDA, and specifically within CDER, how do we support rare disease drug development.
I have the typical disclosures. Just to go over the outline quickly, I'm going to talk a little bit and give you an overview of rare diseases and orphan drugs, talk about orphan drug development, talk about some of the special challenges that we see in rare pediatric diseases.
Then I'd like to talk specifically about the Rare Diseases Program within CDER, which I am a part of, and then another topic I know of interest to people is the rare pediatric disease priority review vouchers.
So what is a rare disease? Probably most of

you know, it's defined by the Orphan Drug Act that was enacted in 1983 to help encourage drug development for rare diseases by incentivizing them. The Act defines a rare disease within the United States that affects less than 200,000 people. These tend to be challenging drugs to develop because of the small numbers of patients that are eligible to enroll in clinical trials.
They're a highly diverse group of orders. They affect almost every body system, and I know NIH especially has worked to identify the different diseases, and they've found over 7,000 rare diseases. Most are serious and most have unmet medical needs.
So each disease individually is rare, but when you collectively put together all the people affected in the United States, it's around 30 million people. So it's a significant public health issue in this country.
Just a little bit about the Orphan Drug Act, as I said, it was enacted in 1983. And before it was passed, there were only about 10 drugs that had

been approved for orphan diseases. And since then, we've approved over 500, well over 500 drugs.
So just a little bit about orphan drug development, in many ways, orphan drug development is not that different than developing a drug for a common disease. When you want to study a drug in human beings, you still have to have a clinical investigation.
These investigations are conducted under an IND, which is an investigational new drug application. What that is, when a company develops a new product and they'd like to test it in human beings, they have to submit a data package to the FDA with things about the animal testing that's been done to show that we have some idea that this is probably going to be safe to give to people, something about the drug quality, how is it developed, how do you know that the drug is a stable drug so it will always be the same drug given.
Once the FDA receives the IND application, we have about 30 days -- not about, exactly 30 days

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to review it. And after 30 days, whether you hear from us or not -- if you don't hear from us, you can go ahead and use it, but otherwise, if there's anything that's questionable, we'll put the IND on hold until the issue is resolved.

An important note is that the Orphan Drug Act does not define a separate regulatory standard for rare diseases versus common diseases. The same level of effectiveness and safety has to be demonstrated for us to approve the drug.

Orphan drugs, the gold standard is two adequate and well-controlled trials with the drug, but oftentimes, for rare diseases, the populations are very small, so we sometimes accept one adequate and well-controlled trial with supporting evidence.

The FDA's required by law to exercise its scientific judgment to determine how much data and information it will take to ensure the safety and effectiveness, and we try to be as flexible as possible for rare diseases because we know of the challenges involved.

Now, most rare diseases, many of them,

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affect children. There are special issues in developing drugs for children, but especially for children with rare diseases. Many rare diseases have phenotypic diversity within a disorder, which means that the disease presents differently in different populations.

This sometimes is due to genetic subsets, that there's slightly a genetic slight difference that causes different forms of the disease to manifest. We're often lacking validated endpoints, outcome measures, biomarkers. They just haven't been developed yet. And oftentimes, there's no drug precedent.

So for many rare diseases, no drug has ever been developed, so the first time it comes to the FDA, that's the first time we're seeing something for this disease.

Also, when you're developing drugs for children, there are many ethical considerations for enrolling children in clinical trials. We have special concerns about protecting the safety and the innocence of children, and yet we want to

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develop safe and effective drugs for children, so you have to do clinical testing.

A couple of things, pediatric research studies should pose no more than minimal risk, and the risks need to be justified by the anticipated benefit. Another thing is that, especially when studying very small children, we need to rely on parents to consent and for the parents to understand what the risks are involved, and then they have to make a decision for their child. But then we also want the children to offer assent, which means just their verbalization or somehow communicating that they're willing to participate in the study.

Now I'd like to focus a little bit more on the Rare Diseases Program. This was a program started in CDER's Office of New Drugs. There was a need for a program to really focus on the issues related to rare diseases. It was formed in 2010, and our mission statement is that we try to facilitate, support, and accelerate the development of drug and biologic products for the treatment of

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patients with rare disorders.

A question we get a lot is what is the difference between the Office of Orphan Products Development and the Rare Diseases Program. These are the two kind of big rare disease groups at the FDA.

The Office of Orphan Products Development, or OOPD, they administer the Orphan Drug Act. So they work with orphan designations, orphan exclusivity, and they also have a grants program both for orphan grants as well as they just started recently a natural history grants program. They also work on rare pediatric devices and humanitarian use device program. Another thing, they work with rare disease stakeholders.

The Rare Disease Program, in contrast, really are not involved in orphan designation or the grants, but we communicate within CDER within the review divisions. We focus on complex regulatory requirements for INDs, NDAs, and BLAs. And we work to develop policies and procedures, including guidances related to rare disease drug

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development.
A couple areas where we overlap is that both groups coordinate across the FDA centers and offices. We have formed something here at the FDA called a Rare Disease Council that has representation from all the different centers and different groups involved in rare diseases.
We work with outside stakeholders. Both groups try to enhance the rare disease information on the FDA website, and we meet together to talk about that and develop the information, and we meet together to work on policy issues.
This is the current staff in the Rare Diseases Program. At our table in the back of the room, you can meet the associate director for rare diseases, Jonathan Goldsmith. Then there's five of us, five additional employees that have different roles and responsibilities within the group, and we hope that this program continues to grow.
Some of the projects, I'd like to talk to you about some of the things that we're doing within CDER. We have several guidances under

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development related to rare disease drug development. Those will be forthcoming. You'll hear more about those as they get published.
We work with senior staff here at the FDA regarding rare disease projects and policies. We work on the Rare Pediatric Disease Priority Review Voucher Program and administer that within CDER, and I'll have some slides later that go into a little more depth about that program.
Another important thing is that the foundation for rare disease drug development is good science. So we try to do what we can to support the development of a good scientific foundation for rare disease drug development. We've developed a database here where we track the rare disease drugs and a lot of different information about each drug. We also work on peer-reviewed publications.
We try to work collaboratively with our stakeholder groups in the community. We work closely with NIH. We participate in the annual Rare Disease Day that happens every February,

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usually on the 28th of February, except for leap year. Every five years, we get February 29th, the rarest day in the calendar.
We participate as panelists in the patient-focused drug development meetings that you've heard about. And we have face-to-face meetings with patient advocacy groups, often collaborating with PASE, and with our colleagues in OHCA, and sometimes the orphan drug group.
We give presentations to stakeholder groups when requested. One of our major stakeholder groups we work with is the National Organization for Rare Disorders, and we always help them plan their big annual meeting that happens in October. I believe it's October 16th and 17th this year. It'll be happening in Washington, D.C. We respond to many, many queries from both internal and external stakeholders.
Rare diseases are complicated, so we get questions from the review divisions. We get questions from people developing drugs. And sometimes, we don't have the answers, but we are

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more than willing to try to steer you in the right direction or connect you with the right people at FDA because we know how challenging it is to navigate the system here. Also, we're a member of the FDASIA Section 1137, which had to do with patient participation in medical product discussion.
Another important thing we try to do is to promote consistency in innovation and review. We hear a lot from industry that they think the different review divisions have different ways of reviewing drugs, so we do whatever we can to attend the meetings for rare disease drug development, and to be part of those meetings, and to try to ensure that there's as much consistency as possible.
We've also developed a rare disease drug training course for the review staff here, so once a year -- it's actually happening next week -- we have a full day of training for all the CDER review staff. And then we also have presentations to numerous professional societies.
One of our most recent projects is that

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we've developed an European Medicines Agency and FDA rare disease cluster. So this group meets once a month. It's a telecon that happens with colleagues in Europe, colleagues here at the FDA, and we discuss topics of global interest in rare diseases.

Sometimes these are higher-level topics and sometimes they're very specific to a specific drug. We have a memorandum of understanding that we can share confidential information between Europe and us. So we talk, how are you thinking about this, how are you thinking about this endpoint, or where are you at in the approval process, and we try to better understand each side of the ocean's thinking about a certain topic.

This slide just shows a little bit about predicting the future for rare disease drug development. Prior to sending in a new drug application or a biologics licensing application, people can apply for an orphan designation. An orphan designation, you just have to show that this is for a disease that's a rare disease and that

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there's a plausible reason that this probably will work for the rare disease.

So this graph shows, from 1983 up through 2016, you can see there's three data points, '83 to 2001, 2002 to 2008, and 2009 to 2016. And the blue arrows define where those three periods are.

We've gone from the first period of 59 drugs being designated as orphan to this most recent period of 2009 to 2016. It's gone up to 248 orphan designations. So this shows that there's a lot of interest in rare disease drug development, and this is where a lot of the work is happening.

The last topic I wanted to talk about was the Rare Pediatric Disease Priority Review Voucher program. This was established in 2012 with the FDA Safety and Innovation Act, and it provides an incentive to encourage the development of drugs in biologics for the prevention or treatment of rare pediatric diseases.

So once the drug is approved at the FDA, the sponsor of a rare pediatric drug, they can be eligible to get a voucher. This voucher is

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redeemable for another review down the road, but that review can get a priority review, which means it will be reviewed in six months instead of the standard 10 months, but it can be for a common disease.

So drugs for common diseases get a standard review of 10 months, but if you have one of these vouchers, you can cash in the voucher. And it could be a new drug for diabetes or for hypertension. But you'll get a six-month review. So this is of a lot of interest to industry.

To get one of these vouchers, it has to be for a rare pediatric disease. The definition was changed fairly recently. It's for a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals from birth to 18. And greater than 50 percent of the disease-affected population has to be pediatric. It has to be a rare disease, so it has to affect less than 200,000 people. And you have to have done clinical studies where you actually studied the drug in children.

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The candidate drug or biologic product that you're developing has to be a new drug. It cannot have been approved before. This is to innovate new drug development. And you can't seek an adult indication for a non-rare disease or a different disease from the rare pediatric disease at the same time. And when you submit it to the FDA, it has to be eligible for a priority review itself. So that means that we have to deem that this is for serious disease with unmet need, and we're going to give it a six-month review.

So far, the program's been, I think, fairly successful. Ten vouchers have been awarded to date. One of the aspects of the program is that you can sell the vouchers. So this has been another motivator for industry, and they've sold for up to $350 million, so it's a lot of money we're talking about. So far, three of the vouchers that have been awarded have been redeemed for priority reviews for other drugs.

We have a guidance, once again, like Michelle showed you. There's a Rare Pediatric

Disease Priority Review Voucher guidance that has more information. And if you have any questions about this program, once again, we'd be more than happy to answer questions.

So I thank you for your attention. There's my e-mail address. And like I said, anyone from our program at any time, we'd be more than happy to communicate with you. So thank you.

(Applause.)

Questions and Answers

MR. BAUER: Are there any questions? Hello, Jen.

FEMALE AUDIENCE MEMBER: Good to see you again, Larry. My question is, can you comment on the Rare Disease Council, how this evolved, who serves on the council, mission and goals?

MR. BAUER: Sure. Yes. So the Rare Disease Council, I don't think you hear much about outside the agency. But what happened was, when the Rare Disease Program began, we found that we were having individual meetings, like our program would meet with CBER, the staff at CBER that were working on

rare diseases. We'd have a t-con, what are you doing. Then we'd have a monthly meeting with the Office of Orphan Products Development. Then we'd talk to OHCA. We'd talk to all these different groups. Then we thought, why aren't we just meeting together once a month?

So the membership, we have representation from CDER, CBER, CDRH, from PASE, from the Patient Affairs and Stakeholder Engagement, from OHCA, the Office of Health and Constituent Affairs. We have group membership from the Office of Legislation. I think that's most of the people, yes.

We meet once a month, and we develop an agenda about what's current. Each group reports off on what approvals they've had recently or any meetings of interest coming up. And then we talk about topics that are of broad interest to the rare disease groups here.

MR. WHITE: Good morning, Larry.

MR. BAUER: Good morning.

MR. WHITE: My name is David White. I'm a patient advocate with the Kidney Health Initiative.

I'm kind of new to this, so if this is a dumb question, I apologize. But you mentioned the need for ongoing assent with the -- being different for the -- is it different for the pediatric population than the adult population?

MR. BAUER: I think assent -- in the adult population, when an adult signs a consent form that they are willing to participate in study, their consent contains their assent. You understand that if an adult, who has their adult consciousness, if they are agreeing to participate in a study, at the same time they're assenting to it.

A child maybe has never been really fully asked, do you understand the study, do you understand the risks. They might just be too small to understand that, but they also have the ability to say I'm willing to do this, whatever it is.

You have to kind of explain to a child in terms that they can understand, and they have to on some level be willing to go ahead and participate in the study. Children have a right to say I absolutely don't want to do this, this is too much,

this is too painful. Thank you very much.

(Applause.)

DR. WHYTE: Again, the Rare Disease program has a table in the back, and they're the ones with the candy, so please go see them.

At this time, I'm delighted to welcome Noah Goetzel from our team, who is an ORISE fellow, who is going to have some audience response questions. And Noah, you might be familiar, he does a podcast for the Washington Wizards.

So how are the Wizards doing? Is it over? I don't know.

Audience Response Questions

Noah Goetzel

MR. GOETZEL: Good morning, everybody. How are you doing? Thanks for the warm welcome, John. The Wizards are still playing. They're fighting for their play-off lives tonight, and they've got a big game before us.

Larry didn't tell you before he started, but there is a test afterwards. And I'm going to ask an audience response question related to the

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material he just covered.
First question, what is the Rare Disease Program able to do? There are a couple of options. The Rare Disease Program at the FDA can do which of the following? Provide training to medical reviewers on rare disease drug development; B, collaborate with NIH, National Institute of Health, to accelerate drug development; C, Rare Disease Program works interactively with rare disease stakeholder organizations; or D, works to speed review and approval of drugs to treat rare diseases? Last option is E, all of the above.
I'll give you guys a couple of seconds to chime in your responses.
(Audience answers.)
MR. GOETZEL: Smart group we have here. Ninety percent said all of the above. That's the correct answer. All of those are roles of FDA's Rare Disease Program.
Next question, which of the following factors does not go into consideration when the FDA is considering which drugs to approve? Biological

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marks is A; B, patient-reported outcomes; C, company stock prices; or, D, clinical outcomes.
I hope you guys get this one.
(Laughter.)
(Audience answers.)
MR. GOETZEL: You got it, company stock prices not a factor for drug approvals.
Next question, if a drug shortage strikes, the FDA can do which of the following, manufacture more drugs to meet the demand; import drugs from foreign countries; force a manufacturer to produce more drugs; or D, none of the above?
(Audience answers.)
MR. GOETZEL: Let's see what we got for the results. So the answer is B, import drugs from foreign countries. About a quarter of you guys got that one.
Now we're on to our final question of this audience response answer. If you're prescribed certain prescription medications, it is legal to buy them online, true or false? A is true; B is false.

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(Audience answers.)
MR. GOETZEL: It's about 50/50 in your results. The answer is true. If you're procedure those medications, it is indeed legal to buy them online. Thank you so much, and I'm going to turn it back over to Dr. Whyte.
(Applause.)
DR. WHYTE: I want to give Noah a lot of credit. Noah's only been here for about three months and really has taken the lead, and writing all those questions.
So see how much you can learn just from a short period of time? Here he is, a young guy who has chosen to come to government to work, and has come to the FDA, so yes. Let's give him a round of applause, and it really is doing a terrific job here, and we're lucky to have him.
(Applause.)
DR. WHYTE: So I'm delighted to welcome to the stage Rea Blakey. I've been fortunate to have worked with Rea in a variety of roles probably over the last, I'll say, 15 years. And I'm delighted

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that she's joined me here at the FDA.
Now, you may remember Rea was a long-standing reporter on a local station, Channel 7, here in the Washington, D.C. area, and then was at CNN, and worked with me at Discovery Health Channel as well as Discovery Channel.
Her fun fact is, while she was a medical correspondent at CNN, Rea's name -- and people always get her name wrong as she says -- it's R-E-A -- was used as the answer to a New York Times crossword puzzle clue.
So I'm delighted to introduce Rea Blakey, who's going to moderate a panel, and really deserves a lot of credit to her and her team for really pulling the day together. Rea has done a superb job. So thank you, Rea.
(Applause.)
Panel Discussion – Rea Blakey
MS. BLAKEY: Hi. Good morning, all. I'm going to ask the panelists to step up, please, so we can all be together at once.
Is everyone enjoying themselves, learning a

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lot? That's most important, learning a lot.
No? No one's learning anything.
(Laughter.)
MS. BLAKEY: Is the mic on? It's because I have this weird sound to my voice. I'm having an allergy reaction over the last couple of days. And you've probably seen a commercial about someone called The Muddler. That's me today.
So forgive the quality of my voice, but I'm sure that you will enjoy the content from our panelists. I am really thrilled that they've all joined us today because these are people we interact with at Professional Affairs and Stakeholder Engagement on a regular basis.
Quite honestly, if we weren't a whole community, we wouldn't get nearly as much done. Sometimes, occasionally, we step over top of one another, but we pretty quickly sort it out, and we're very fortunate to have a collaborative effort that exists here.
So I want to just extend my personal thanks to each of you for participating even though you

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haven't heard any questions yet. And I did promise them that I wanted this to be a very interactive session. And by that, I mean you can't just sit there. That's what interactive means.
So I might throw in a pop quiz question for the audience. I might ask a speaker to address something that maybe they weren't prepared to do, but only if the audience doesn't participate, so it's really on you as to how much pressure is placed on them. Got it? Then we'll know if you're truly friendly. Oooh, it could be tough.
All right. Let me ask a question. How many of you would like to have your voices heard? Show of hands, please.
(Show of hands.)
MS. BLAKEY: There are some people who are not raising their hands. So that intrigues me. But for those of you who would like to have your voices heard, you have come to the right session. This is exactly what this panel is about. And a lot of it has to do with the fact that we're the people oftentimes on the front line of engagement

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when it comes to CDER and the FDA.
So without further ado, I do want to introduce the panel. And let me just say that there is that constant disclaimer that you've heard before. This goes for all the panelists, that the opinions expressed are personal, do not specifically represent the FDA.
Given that, let's start with Dr. Lynne Yao, who is farthest from me. She's the director of the Division of Pediatrics and Maternal Health. She and her staff led CDER's efforts toward informed use of medicines in children and women. And I know that that's of great interest to all of us, but they're a specific sort of in-house consultant group that we use here. So it's really important to have Lynne and her team participate.
Also, you did a public workshop maybe last year. Maybe you could tell us a little bit about that as part of your comments.
Next to Lynne, we have Pujita Vaidya, who is the acting director of the decision support and analysis team. That's part of the Office of

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Strategic Programs. We collaborate a lot at PASE with OSP, and one project in particular we're really happy about, we'd love to tell you about today, but you'll have to come back and check our website because we don't really have all of our information available. But that's just a little tease to make you come back.
Pujita's going to talk a lot today about externally-led patient-focused drug development meetings. And I know that's an interesting topic for a lot of you.
Next to Pujita is Chris Melton, who is my colleague. You heard Chris introduced earlier today. He is a health communications specialist. And he's going to represent the perspective of PASE, what we're doing in our office and how we engage with you as stakeholders.
Closest to me, Andrea Furia-Helms, who is with the Office of Health Constituent Affairs. I'm going to use a little pop quiz question here, Andrea. I hope you're all right with that.
Her office actually also received recently

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an award for, let's see, patient representative training workshop that they had put on. So they're very deeply embedded in patient engagement here at FDA.

But the pop quiz question, which is for the audience, has to do with a particular drug development issue. It's a drug, in fact, that's used to treat HIV and AIDS. It was first synthesized as a potential anti-leukemia drug, but it didn't work. However, it was found to be active against a retrovirus, which led government researchers to consider it as an HIV fighter. The drug was approved in 1987.

Who can tell me the name of the drug?

No, Larry, you can't.

Anyway, you can just yell it out, who doesn't work at FDA.

MALE AUDIENCE MEMBER: AZT.

MS. BLAKEY: AZT. Thank you.

There are going to be more pop quizzes for you folks because I need a little bit more energy from you. And that brings me to this interesting

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little tidbit. Your office really came about almost as a result of all of that activity during the early '80s.

Andrea, take it away.

Presentation – Andrea Furia-Helms

MS. FURIA-HELMS: Good morning, everyone. Thank you for coming today. Thank you, Rea, and thank you for PASE's inviting OHCA, the Office of Health and Constituent Affairs here today.

I want to start today with just a little bit of overview about our office. Our office is located in the Office of the Commissioner, and we have been around for, as Rea had mentioned, quite some time.

We started in the late 1980s in response to the HIV-AIDS patient advocates protest outside of the FDA headquarters at that time. And they were concerned because FDA was taking a little bit longer than they anticipated for reviewing and approving new therapies for them. And at that time, that's when FDA realized we need an office to work with patient advocates, and really talk to

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them regularly, and include them in the process.

So our office is an office of patient engagement and assistance. We assist you all in navigating FDA across the medical product centers. We work with devices, drugs, and biologics. So if you have an issue that you don't know where to go, you come to us, and we help navigate for you. We help you connect with the appropriate people. We help you get meetings and to meet with the appropriate people to address your concerns and get your voices heard internally.

We are basically advocates for you all. As you are advocates for your patient communities, we are advocates for you internally, and we work to include your voices in regulatory processes. We look at different activities and meetings that we feel that the patient voices could be useful, and we work to get those voices heard for you.

This is just to show some milestones of patient engagement over the years at FDA, as I mentioned it starting in the late '80s. Things to note is the FDA Patient Representative Program,

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which I'll be talking to you mostly about today. That started in 1991 when the first patient representative served on an anti-viral advisory committee for an HIV-AIDS drug.

Then that's when the cancer advocacy community said, hey, we require a voice, too. We want a voice at the table as well. So we really opened it up to all serious and life-threatening diseases at that point. And we fought for patients to have a vote on advisory committees in the mid-1990s.

In the early stages of the Patient Representative Program, the patient representatives were not voting, and they weren't allowed to review the confidential information. But our office fought for that, so now patient representatives have an equal vote as the scientific members.

In recent years, we've expanded patient engagement as you can see, not only a broader inter-office with the FDA patient network, which I'll touch upon later, but also, as Pujita will be speaking about, the patient-focused drug

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development, and then other center-specific activities that have been occurring.

So as I mentioned, the Patient Representative Program began in the 1990s. Really, the goal is to have the patients have an active role in the advisory committee process and the review division meetings. So there are certain meetings that occur early in the drug development process that patients can have a voice in as well, and the Patient Representative Program also provides that voice as well.

So the patient voice is a representative in these important decision-making meetings for regulatory issues. And I think it's important to note that having a patient at the table humanizes the process. It reminds us that these are folks that are the end users of the products, and that's what we have to keep in mind.

So who are the patient representatives? They're patients that have experience with the disease or condition, primary caregivers to patients such as spouses, family members, even

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friends. And they're usually members of patient advocacy communities and are involved in patient advocacy groups.

Our patient representatives have to become special government employees. That's a temporary government employee status. So we're regular government employees, and this is sort of a temporary status, but they do go through conflict of interest screening, just as we do as regular government employees. Currently, we have over 200 patients and caregivers serving in the program, and they represent over 300 diseases and conditions.

We have a recruitment process, and we recruit based on need. We know that advocates want to advocate. They want to act. They want to do things. They want to make an impact. So we want to make sure that the patient representatives that we recruit will have an opportunity to serve within their four-year appointment.

It's usually that we recruit because there is a product in development, and we need a patient voice and a patient perspective in that particular

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product, or there's a product application in house for FDA to review. And once they're on board, we immediately start training.

There's preparation and training involved in terms of an FDA 101, where we provide a high-level overview of our regulatory processes, our organizational structure, and really to address some misconceptions and misinformation about FDA and what already is and is not.

We have regular webinars and also an annual patient representative workshop, which we have every July. And that brings in the newly recruited patient representatives to learn about the medical product development life cycles, conflict of interest. Because advocates are out there advocating during their activities, being a special government employee, some of the activities can conflict them out of serving, so we have to provide specific training on that.

Mentoring by senior patient representatives, the newly recruited sometimes are a little intimidated before their first meeting with FDA and

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the sponsor, so we connect them with the senior patient representatives to sort of ease their mind about how to prepare, what to expect. And that's been very helpful to them.

What this training does not only prepares them in serving, but it also furthers an understanding an appreciation about FDA's regulatory processes. And they go back to their patient communities and they provide education as well. As I mentioned, there may be some misconceptions and misinformation out there about FDA's regulatory authority for example.

So that education and training that we provide them also helps them provide that information to their community.

So we have a legal basis for continuing and broadening our patient input in recent years. The FDA safety and Innovation Act of 2012, Section 1137, which Larry had mentioned earlier, patient participation and medical product discussions, is the legal basis for us to find ways to include the patient voice earlier in the

development process.
What has been done so far since that has been signed into law is we created a cross-agency workgroup to discuss how to implement this. And we decided we should open a docket in hear from our stakeholders, from you all. How should we implement it? What are your recommendations and suggestions?
So from that, we pulled all the comments together, and there's a stakeholder view summary report on our website. We have ongoing activities, as you all know and you're probably involved in. There are centers that are implementing their own activities, and we continue to do our activities as well in OHCA.
But from that cross-agency workgroup that was initially formed, now we've evolved into a patient counsel. So now, because there are so many activities and so much going on across the centers, we're working together to better inform each other, and to leverage off each other when we have patient engagement activities, and really to know what's up

and coming.
So from FDASIA 1137 and from that stakeholder views report, one of the suggestions that we heard you, and we listened, and now we're taking action, we're developing the Patient Engagement Collaborative, and we're working with the Clinical Trials Transformation Initiative on this.
This is going to be an external group of stakeholders such as yourselves that can participate in regular meetings with FDA to talk about how can we enhance patient engagement at FDA.
It seems to have been an explosion over recent years about patient engagement, which has been fantastic, but we sort of want to make sure we're going in the right direction and that maybe there's some things we could be doing better.
So currently, that's in development, and we are going to issue a Federal Register notice for a call for nominations, hopefully soon. There's been a little bit of a hold with the transition in administration, but once that comes out, I

encourage you to apply if you're interested. If you have any questions, I'm happy to answer them.
But that's all I have.
MS. BLAKEY: Wonderful. Thank you, Andrea.
All right. Is our audience still with us? I think it's time for another pop quiz. Put your thinking caps on. This particular drug is used to treat estrogen-positive breast cancer, which accounts for 50 to 70 percent of cases. It may also prevent the development of breast cancer in high-risk patients.
It was originally intended as an anti-fertility drug when it was synthesized, but it turned out that it stimulated ovulation instead of suppressing it.
Who has a guess at what this drug is called? Tamoxifen. Perfect, wonderful. Okay. I have one person who is definitely with me in sync. Thank you so much.
Just for that, I'm going to try another one, and I bet more of you can get this one. This particular drug first appeared in the market in

1979 as a breakthrough for high blood pressure, however, it increased body hair growth for 80 percent of patients.
You don't have to wait if you know the answer. The drug is?
AUDIENCE MEMBER: Rogaine.
MS. BLAKEY: Thank you. Wonderful. Congratulations. Fantastic.
All right. I got them warmed up, Chris. Now it's your turn to talk about what we do in Professional Affairs and Stakeholder Engagement that would be of interest to this audience.
Presentation – Christopher Melton
MR. MELTON: Rea, thank you for the introduction.
What's important in what we do with Professional Affairs and Stakeholder Engagement, we are a conduit to start two-way engagement. And I know you've heard a lot of acronyms, and Dr. Throckmorton in the beginning speak as far as a culture change within PASE. We are here to be a conduit for two-way engagement. So if there are

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any questions that you have regarding who would I speak with, you would come here with us in PASE.

Also, we have at least five top issues that we've been working on, one of them being patient advocacy groups and stakeholder meetings. In 2016, we have had over 104 meetings, and most of those have been with external stakeholders, and that was a 30 percent increase over 2015.

But the basic point, what I would like to get across to the audience, is that the Rock the Docket, that's a good key initiative to start the process because, as you've heard and will hear throughout the day, you'll hear Federal Register notice, docket, this is a way to start the communication. And once you have that starting point, then from there it can continue to grow. And again collaboration and us being able to have open communication will really work the best for us to continue on. And that's it for me.

MS. BLAKEY: Which is fine, because we want to leave plenty of time for questions and answers. So that was a very lovely introduction. We move

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down to Pujita, who wants to talk a little bit more about the externally-led PFDDs, among other things.

Presentation – Pujita Vaidya

MS. VAIDYA: Hi, everyone. I'm Pujita Vaidya, as Rea mentioned. And I'm in the Office of Strategic Programs in FDA's Center for Drug Evaluation and Research.

Today, I'll be talking to you about the Patient-Focused Drug Development initiative overall. This is an initiative that I've been a part of for about five years now, so from the very beginning, I've been involved in this work. So it's pretty near and dear to me, I would say.

I just want to put a disclaimer. I know Michelle has introduced some of this stuff, so some of the slides may be similar. I'll try to switch it up a little bit and just give a quick overview, and then mainly focus on the externally-led patient-focused opportunity here.

So as we've heard from a lot of folks today, people living with the condition have a direct stake in the outcomes of drug development, and they

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have a unique ability to contribute input and can inform drug development and evaluation.

So FDA recognized that there is a need for a more systematic way to collect and gather this patient perspective that can inform drug development overall. So what we came up with in PDUFA V, which is the fifth authorization of the Prescription Drug User Fee Act, is the Patient-Focused Drug Development initiative under which we are conducting 24 meetings, which are specific to certain disease areas.

So here, you can see the list of different diseases that we have focused on, and we have two remaining for this fiscal year, which will close up PDUFA V.

At these meetings, I would say, overall, the disease area is here. You can see diseases are chronic, symptomatic. There are several rare diseases as well in our list here.

Typically, at these meetings, when you attend the patient-focused meetings, you'll get about, I would say, anywhere -- we've ranged from

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30 to about 80 to 90 patients or patient representatives that attend the meeting, overall attendees, so other folks, I would say. But in total, we would say about 100 to anywhere, 150 total participants. And then we have similar numbers on the webcast as well at these meetings.

The meetings that we have are focused on two main topic areas. So the main discussion is focused on gathering patient perspectives on patient symptoms and its impact on daily life, and also patients' perspectives on current approaches to managing their condition.

So the types of questions we ask are, which substance has the most significant impact on your life, how does it affect the ability for you to do specific activities, how well do your current treatment regimens treat the most significant symptoms, what are some of the things that you look for in an ideal treatment, and we also delve into discussion about, in some cases, what factors do you take into account when making decisions about treatments.

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So these are the types of questions that we cover and the discussion that we have in a large group-facilitated discussion.

I would say one of the main things that we have realized is that active outreach is the key to success, and that's where patients, stakeholders, and advocacy groups play a very important role.

We have seen in several cases, in preparation for these meetings, that advocacy groups have taken initiative to coordinate efforts, whether it's helping with outreach through social media, through the contacts that you all have, because we actually here at the FDA, we don't have the direct contact with the patient themselves. So you're the ones who hold the key to that database, let's say.

Along with that, some have organized for these meetings. Some have organized patients, transportation, buses to actually bring patients and patient representatives to the White Oak campus. As you've probably realized today, it's not easy to come here and get to this location. So

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they have organized that. They have organized pre-meeting get-togethers, sometimes even webinars to prep folks for these meetings.

One of the main things, as we've learned, I would say, is these meetings really strengthen the understanding of the disease and treatment burden. As Michelle mentioned earlier, each meeting results in a voice of the patient report that faithfully captures the patient input from the various information streams.

So through the webcast, what we hear at the meetings, through the docket, as you've heard about, where a lot of people are able to submit their comments after the meeting as well, that input can support FDA staff and benefit-risk assessment and also in thinking about clinical outcomes assessments as Michelle mentioned.

Another thing that we think is -- the patient input collective can value drug development more broadly as well. So in cases, it can help identify areas of unmet need in the patient population, help identify or develop tools and

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assess benefit of potential therapies, and also help raise awareness and channel engagement within the patient community overall and educate.

Now, I'll talk to you about the externally-led patient-focused drug development opportunity that we have. There was a growing interest, external interest in expanding the efforts to gather patient input in support of drug development and evaluation.

About two years ago, we started welcoming patient organizations to identify and organize their own patient-focused collaborations. These meetings are truly your meetings. FDA, I would say, in the part of the planning part, we don't have a lot of input, and we leave that all up to you. And any resulting products from these meetings, we also say -- let's say, any reports, surveys of actual meetings. Those are not FDA-endorsed or sponsored. So these truly will be your meetings that you are conducting to gather this information.

We have realized that the success of an

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externally-led patient-focused meeting really requires a joint and aligned effort by multiple advocacy groups associated with the disease areas because in some disease areas, as you all know, there are several groups that are involved for one particular disease. So it's nice for everyone to come together and look at opportunities to conduct these types of meetings.

Now, I'd like to go over some considerations and things to think about as you're planning a meeting. What we realized here and from our own meetings, and what we would like to share, is that the key participants and the voices that we want to hear at these meetings are from patients, patient representatives, meaning caregivers or parents who are directly affected by this, and then patient advocates as well. Those are the key -- it's really a platform to hear their perspectives.

The target audience, in addition to them, I would say, who are mostly in listening mode, would be your regulator, the regulatory, federal agencies like the FDA folks, medical product developers, so

drug developers, device developers that are there.
They're important to have in the room because they're the ones who will go -- and from what they hear in the meeting -- let's say, something about endpoints. If we're hearing something from patients about you're really not focusing on the core symptoms that I think is most meaningful to me, they're the ones who can go and start thinking about it further, researchers and healthcare professionals.
What we've tried to do is from the 22 meetings that we've conducted so far, we want that to kind of help serve as a model in identifying targets in disease areas to have a meeting in the main topics that I mentioned earlier, focusing in on those two topics, exploring this structure and format of using a facilitator-led large group discussion, having an interactive webcast and other discussion aids like polling tools like we're using today.
Meeting deliverables are always very helpful because if for some reason let's say you have

folks, you have drug developers, you have folks from the FDA staff who are for some reason unable to attend the meeting, it's good to have a web recording available, or a transcript, or a summary report for them to refer back to later.
One thing I do want to mention is that these meetings do not have to be a stand-alone meeting. So we really encourage you to consider taking the style, and understanding the style, and incorporating it into other opportunities. A lot of groups have annual conferences. They also have maybe sometimes a scientific workshop.
There may be an opportunity to actually add a session, a two-hour session maybe, to that to kind of gather the patient perspectives there. So it doesn't necessarily always have to be a half-day meeting or a full-day meeting.
We do have a letter of intent process where we ask that you submit a letter of intent to the Office of Strategic Programs. It is really just so that we know that this meeting is taking place so that we can serve as a helpful resource to you.

Since we are the ones who have been leading this effort for the past five years, four and a half years now, we have learned a lot, and we are able to guide you through the process.
We understand, like I said, that since we're a team of five that leads this, and we're the ones who conduct the meetings along with the other projects and initiatives that we work on, we really understand that it takes a lot of effort. But it does not need to be resource intensive.
So you may not necessarily always need to have a meeting planner or a scientific writer for these meetings. That's where we want to try to help to at least serve as a resource so that we can guide you through your planning.
As I mentioned earlier, active community outreach is key to ensure a representative group of patient perspectives are actually in the room. So that's very important. And at the end of the day, I think the main thing is we want to be respectful of the time of patients, and caregivers, and patient advocates, and groups out there.

Here is just some more information. We have all of our stuff on our FDA website. The externally-led page has guidelines on the letter of intent process. If you have any questions, please e-mail us to our patient-focused box. Thank you.
MS. BLAKEY: Thank you, Pujita.
Dr. Yao, I'm going to give you the last word on the panel for now, and then I would encourage those of you in the audience who have questions to not only formulate them quickly, but to come toward a microphone or raise your hand so that we can incorporate those questions as part of the discussion. I don't want us to run out of time.
Dr. Yao, you want to talk a little bit about what goes on in your office?
Presentation – Lynne Yao
DR. YAO: I'm going to talk very briefly, which for those of you who know me is a real struggle. But Rea has the stick. She can just show it to me, and I'll know I need to get cut off.
I really want to be brief because we really are here this morning to hear about questions that

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you might have about how you get your voice heard. I'll just give you a couple of examples, and then I want to hear from you. We all want to hear from you.

The first is this image that I was given of a cartoon of a castle with a big wall around it, and a moat, and alligators, and you see someone lobbing with a catapult something over into the castle.

That's the view that many people used to have of FDA, and some of you may have right now, that there's this gated-off castle where it's impossible to penetrate. And if I want to get something heard or I want to have my voice heard, I've got to throw something over the wall and see if ever something gets thrown back over.

What you've heard this morning, I think, is not just that we are interested in throwing things back over all the wall, but indeed, we've lowered the gate. We've taken our first tentative steps out there to meet you, and we want you to come on in. Okay?

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All of the initiatives that you've heard are efforts to do that. Some of them are very formal. Some of them are less formal. But all of them are intended so that you can get your voice heard. And we are very, very interested in the Office of New Drugs and the Center for Drug Evaluation and Research to hear your voice.

The only other thing that I want to say is that patients matter. Patients matter. If it weren't for patients and families, we would not exist. My background is in pediatrics, and I want to leave you the one story that has to do with a question that arose about the difference between assent and consent that I heard.

I had a patient when I was an intern who had a very unfortunate aggressive form of leukemia, acute myelogenous leukemia. And Jonathan was going through treatments. His parents were very concerned. He was an only child, only five years old. And because of this great program called -- what's that program?

See, now I'm going to forget now -- where

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kids get -- Make A Wish. It was the Make A Wish Foundation. Jonathan and his parents enrolled. And it was their deep desire for Jonathan to meet his grandparents in Korea because he had never gotten a chance to meet.

So his parents had coached him, and coached him, and coached him because they were going to get interviewed about what Jonathan's wish would be. So they said, "Jonathan, what do you want to do?" And he said to his mom and dad, "I want to go to Korea to see my grandmother." Great.

So they interviewed the family together, and the family said, "Well, we really want to go to Korea to meet Jonathan's grandmother because he never got a chance to meet her." Okay.

So then what they do is interview the child by himself. So when they got Jonathan into the room and they said, "Jonathan, what do you really want to do if you had anything you could do?" And he said, "I want to go to Disneyland!" And the family went to Disneyland.

(Laughter.)

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DR. YAO: So the difference between consent -- and this, again, illustrates why the patient voice is so important.

We know, certainly in children, in the care of children, that there are a lot of things that get involved when you have a serious disease, when you have a chronic disease, when you have a disease that requires therapy, and maybe there's no therapy involved.

The parents are desperate to find a cure or treatment for the child. And maybe the only thing the child really wants is to go to Disneyland. So what we really want to do is get at the heart of the matter, hear the voices, hear the voices of patients, of children, of parents, and develop programs that address all of those needs.

Questions and Answers

MS. BLAKEY: Perfect, perfect.

Now we'd like to hear your voices. Questions, please? Don't be bashful. Someone is approaching. Yes. And it's okay if there's a small line. I think we can probably take three or

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four depending on the length of the responses and so forth. Yes, ma'am?

GINA: Hi. I feel like I'm on the old Phil Donahue show. My name is Gina. I'm the executive director for the Alport Syndrome Foundation. I have a couple of questions about the externally-led meetings, as we are hoping to hold one next year. You mentioned that several advocacy groups would be necessary. If there's only one advocacy group that really covers a disease state, I'm presuming it's okay if we do this.

MS. VAIDYA: Yes, of course. I think the point I was trying to get at is if there are several groups out there, for you to join forces.

GINA: Earlier in the day, it was mentioned, the option of having an online meeting instead of an in-person one. Is that true or did I misunderstand that?

MS. VAIDYA: I don't see why that could not be possible. I'll be frank. We haven't received any requests for that, but I think that would be perfectly fine, yes. The key is to be able to

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reach the population and get the perspectives that you need.

MS. PARZIALE: I wanted to gauge your thoughts on the appropriate role of industry in such a meeting in terms of inviting drug developers to come. Are they able to assist in the costs? What would be considered appropriate for something like that?

MS. VAIDYA: So the role that we see overall in the meetings itself is that usually they're in listening mode at our meetings here, mainly to hear what the perspectives are so that they can identify areas where they may need to go and modify their approach, or think a little bit more about different endpoints.

Now, thinking about the planning perspective, I would say I believe there have been cases in the past where it's perfectly fine to have industry if they are able to sponsor a meeting. And we would suggest that you at least put a disclosure out so that is known.

But at the end of the day, these meetings

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are disease specific, they're not product specific, so it really shouldn't be a big deal.

MS. PARZIALE: Great. Thank you so much.

MS. BLAKEY: Thank you. Yes, ma'am?

JENNIFER: Hi. I'm Jennifer. I just had a question regarding the new patient engagement initiative. You said the nominations would be through the Federal Register. What is the best way, I guess, to be alerted by FDA when the nominations are open? I don't regularly follow the Federal Register. It would be painful to read.

MS. FURIA-HELMS: That's a perfect question.

JENNIFER: What to subscribe to in FDA so you can make your --

MS. FURIA-HELMS: So that's a great question because I'm going to leave some postcards at the registration table. We have a patient network newsletter, and that is your one-stop shop. That comes biweekly to your e-mail with all FDA activities regarding new approvals, recalls, any new activities and patient engagement opportunities, Federal Register notices, dockets

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that are open for commenting.

Everything is there in that newsletter biweekly. So I'd encourage everyone to subscribe to that. We currently have, I think, 58,000 subscribers, maybe 60,000 at this point. But that is your one-stop shop to get that kind of information and be informed of what's going on, very current information.

JENNIFER: Thank you.

MS. FURIA-HELMS: You're welcome.

MS. BLAKEY: Do you mind? Hand the microphone to her. Thank you.

MS. WEST: I have a couple questions. I'm Melissa West with the Kidney Health Initiative. First question, the externally-led PFDD meetings, are they published once you do accept a letter of request? Is that community notified?

DR. YAO: So when you mean published, you mean --

MS. WEST: Are you keeping a list of what you have accepted once you've reviewed?

DR. YAO: We actually do not have that

available on our website anywhere. But we can take that back and see how that's possible.

MS. WEST: That would be great.

DR. YAO: The only way that we've done it is that if you do reach out to us, we could let you know which group has had a meeting or if there are some coming up. They're doing a pretty job of outreach and advertising those meetings as well. So yes. I will definitely take that back and see what we can do.

MS. WEST: That would be great. I'm seeing an opportunity for best practices, especially in the deliverables that are created.

DR. YAO: Exactly, definitely.

MS. WEST: For the Patient Representative Program, is that list publicly offered, or do we have the ability to contact you to determine if there's any of our membership who would be serving in that role? How would we get access to the list of patients, the 300 patients on the patient representatives?

MS. FURIA-HELMS: The list of the patient

representatives are not public, but you can contact me, and we can have a conversation, and see if there is representation. And if not, we can discuss that.

MS. WEST: Perfect. And then my last question is I think there's an open docket right now around a new office of patient engagement. I'm curious in terms of any insight into that or what impact that will have in terms of the various constituency here.

Then I also had a question specific to the Patient Engagement Collaborative that you're working on with city [ph], and what, if any, potential impact. Will that still be on its own track?

MS. BLAKEY: Quickly, she can address the Patient Engagement Collaborative. We really don't have any other information other than the FRN for the first question that you asked, so unfortunately, we don't have anything more to address there, but yes.

MS. FURIA-HELMS: So the Patient Engagement

Collaborative has been in development since summer of last year. We developed with City's patient advocate steering committee members. Some of them have been part of the planning workgroup, and we've developed a framework. And we're in the process of getting that Federal Register notice out for a call for nominations. And it'll have outlined what the eligibility criteria is and things like that.

So that should be up and coming. As I mentioned, it's been a little bit tough to get Federal Register notices with the transition. And we have a new commissioner starting today, so we're really hopeful that that will go soon.

MS. BLAKEY: Just checking the time quickly, I think we just have time for these last two questions if they're brief. So yes, please. I'm actually directing it to you, yes, and the lady behind you.

MEGAN: Hi. My name is Megan. I'm with the Parkinson's Foundation. Thank you for your information that you've provided today. My question was about the PFDD meetings. We were

fortunate enough to have five of our research advocates actually contribute to the 2015 PFDD report. And I was just wondering if there are any specific outcomes that you guys are measuring that are coming out of the white pages that are being published, or if you've seen any uptake or anything like that with those reports.

MS. VAIDYA: The voice of the patient reports are really supposed to serve as a resource for our FDA reviewers, so our OND reviewers and the other reviewers overall.

From what I know right now, I'm not aware of anything. There may be stuff going on that I'm not aware of. But I would say the report itself right now, we would say is serving as a resource to them, to think about the therapeutic context overall. But unfortunately, I'm unable to give any more details on that. Sorry.

FEMALE AUDIENCE MEMBER: Hi. My question is about -- actually, you've mentioned a lot of engagement with rare disease, or not just rare disease, but advocacy groups in the PFDD,

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et cetera. And I'm wondering, do you have any experience working with patient communities for which there is no formal advocacy group, no formal nonprofit representing them? If so, what is it? And if not, do you have any advice for those patient communities that do not yet have that organizational structure to approach the FDA and have their voices heard?

MS. VAIDYA: Let me think back.

MS. BLAKEY: Can I help you with that a little bit?

MS. VAIDYA: Sure.

MS. BLAKEY: That might be an area where you could reach out specifically to Professional Affairs and Stakeholder Engagement. We do deal with advocacy groups as well, but we do have a lot of people who are really naïve to the process. And so if you send an e-mail to either myself or Chris, whose name was actually in the FRN promoting this, we'll be glad to assist you.

Oftentimes, we're able to get you exactly to where you need to be and create the meeting. We'll

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navigate as best we can on your behalf. So we like those more naïve people to come to us so that we can assist.

I think we're probably beyond our time limit, and I thank you all for your time and attention. Thanks for playing the pop quiz. Thank you.

(Applause.)

DR. WHYTE: Thank you, Lynne Yao, for that metaphor of the castle and the moat. We'll use that.

So it is a little after 12:30. We will now take roughly an hour lunch. Let's try to get back here at 1:30. Remember, this is Noah Goetzel, our young ORISE fellow, and Noah's going to help coordinate the teams for Jeopardy when we come back. So go have lunch, get caffeinated up, and not too much sugar, because I don't want you to fall asleep.

We'll come back. We'll have a half-hour of Jeopardy questions. Then we'll hear from our colleagues about social media. And if anyone is

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tweeting things out, let me know. But see you all at 1:30.

(Whereupon, at 12:35 p.m., a lunch recess was taken.)

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A F T E R N O O N S E S S I O N

(1:32 p.m.)

FDA Jeopardy – John Whyte

MR. GOETZEL: Good afternoon. If we could please get the Jeopardy members to come up front, and you will be sitting at this front podium. Team 1 will be Gina Parziale; Rebecca Scott; Angie Onofre; Christa Kerkorian; and Shimere Sherwood. Please come up to the front and huddle around this first seat.

Team 1, one more time: Gina Parziale; Rebecca Scott; Angie Onofre; Christa Kerkorian; and Shimere Sherwood, please come up to the stage.

Team 2 will consist of Calvin Ho; Alyssa Reimer; David White; and Brittany Blocker. Come on up to the stage.

On to Team 3, three of four, we've got Jessica Langton; Kamilah Rashid; Stephen Shaul; and Gay Grossman. Please come up front to the stage.

Last but not least, Team number 4, Caila Brander; Chris Celeste; Melissa West; and Monica Weldon, please come up front. Thank you.

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DR. WHYTE: All right. Thank you, Noah.
Let's get our teams and get ready. I know it's crowded up here, but it's going to be okay. So Team 1 is over there, Team 2, Team 3, and Team 4. So you have to pick one person to be your clicker, and you can huddle together. But we do need someone to sit here who can give the answer and to press the clicker.
This is kind of like drug review, lot of people, lot of activity.
Team 1, we need someone to take the lead. So I want to introduce you to Chad, who is our brains behind all of this and will control everything. To be fair, you're not going to be able to click in until the question is read. Like on real Jeopardy, I think you can click in at any time, but you have to click that on the top pretty hard. We always have people that say their clicker is not working. I'm not going to go for that. You go, hit it hard.
Can we test it or no? Try to test it then. Yes. I think that's a government answer. I

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already checked them. They're all approved. They're kind of like a device.
So may we start, Chad? Now, the computer will randomly decide who goes first. Is that how it works? So the categories are Acronym Soup, Drugs and Biologics, Play It Safe, Trials and Tribulations, and Advocacy Cheat Sheet.
So where is Team number 2? Tell me your name. Calvin, go ahead and pick.
TEAM 2: [Indiscernible – off mic].
DR. WHYTE: IND, remember, in the form of a question. Team 2. Calvin, what's your answer?
TEAM 2: Investigational new drug.
DR. WHYTE: I'm going to need it in the form of a question, Calvin.
(Laughter.)
TEAM 2: What is an investigational new drug?
DR. WHYTE: That is correct. Okay. Choose again, Calvin, your team.
TEAM 2: Play it safe for 100, please.
DR. WHYTE: Low numbers, okay. This center

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of the FDA evaluates new drugs before they can be sold, ensuring generic and brand-name drugs work correctly -- you guys aren't listening; you have to wait until I've finished reading -- and that their benefits outweigh their risks.
Go. Is that Team 2? Yes. Team 2?
TEAM 2: What is CDER?
DR. WHYTE: What is CDER? That is correct. What does it stand for? I'll give it to you, Center for Drug Evaluation and Research. You've got to click right at the right time. You have to wait until I stop talking.
Choose again, Team 2.
TEAM 2: Drugs and Biologics for 300, please.
DR. WHYTE: These type of drugs fill most of the prescriptions in the U.S., although they typically cost less than their brand-name counterparts -- you're not listening -- they're equivalent in terms of quality -- team 1, you're not listening -- performance, strength, and safety.
Team 3?

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TEAM 3: Would that be generics?
DR. WHYTE: Are you asking me or are you telling me? What is your question?
TEAM 3: What is a generic?
DR. WHYTE: Okay. What is a generic? Very good. Team 3, choose again.
Okay. We're waiting.
TEAM 3: Let's do Play It Safe for 500.
DR. WHYTE: Play It Safe for 500. The FDA can require manufacturers to provide this safety strategy to manage serious, known, or potential risks associated with medicines and manage their use so that patients can continue using them. And there are multiple options for this.
Team 1?
TEAM 1: What is REMS?
DR. WHYTE: What does REMS stand for?
TEAM 1: Risk Evaluation Management Strategy.
DR. WHYTE: I'm going to give it to you. What is REMS? That's one of the answers. Correct.
(Laughter.)

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TEAM 1: Risk Evaluation and Mitigation Strategy.
DR. WHYTE: Well, it's right in front of us. Okay.
Team 1, choose again. Now we've got a game going on, people, except for Team 4.
Team 1?
TEAM 1: Advocacy Cheat Sheet for 500.
DR. WHYTE: Advocacy Cheat Sheet for 500. Whoa! How much are you going to -- how much?
TEAM 1: We're going to go all in.
DR. WHYTE: 500, there you go. 500, she said. This organization engages its stakeholders, including patients, advocates, and healthcare professionals to improve their understanding of how the FDA approves and regulates drugs.
Team 1, did you click? Is that right?
TEAM 1: Yes, the PFDD. What is the PFDD?
DR. WHYTE: No. What is Professional Affairs and Stakeholder Engagement? Remember, other people can click in when the -- you could have, yes. Remember, if the first person gets it

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wrong, other people can click in.
But we're going to go back to Team 1 because no one else got it.
TEAM 1: We'll do Acronym Soup for 500.
DR. WHYTE: OND, Team 1? I know. Do it like that. Team 1, you had extra time.
TEAM 1: Office of New Drugs.
DR. WHYTE: In the form of a question.
TEAM 1: What is the Office of New Drugs?
DR. WHYTE: Very good. Team 1?
TEAM 1: Drugs and Biologics for 500.
DR. WHYTE: These products include vaccines, human blood, and blood components, human cells, gene therapy and tissues, gene-based and cellular products within this category at the forefront of biomedical research and may be used for conditions that lack other available treatments.
You tried a new strategy. I didn't think it was going to work.
TEAM 4: What are biologics?
DR. WHYTE: What are biologics. That is correct. And look at you. It works after you said

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it doesn't. And look, you're tied for the lead after complaining.
Team 4, choose again.
TEAM 4: Let's try for Trials and Tribulations for 500.
DR. WHYTE: Also known as compassionate use, this practice refers to the use of an unapproved investigational medical product outside of a clinical trial. Team 1?
TEAM 1: What is the expanded access program?
DR. WHYTE: That's correct. What is expanded access? Very good. Team 1, choose again.
TEAM 1: Advocacy Cheat Sheet for 400.
DR. WHYTE: This program helps consumers and healthcare professionals better understand who takes part in clinical trials by providing them with demographic data on the trial participants for FDA-approved new molecular entities.
Team 3? You do get penalized if you get it wrong.
Anyone else? Chime in. Team 1? It did.

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TEAM 1: What is a clinical drug snapshot?
DR. WHYTE: No. That's not the exact phrase.
Team 4?
TEAM 4: What is clinical trials drugs snapshot, clinical trial snapshot?
DR. WHYTE: It's just, what are drug trial snapshots? You didn't buzz in, he says.
TEAM 4: Oh, perfect.
DR. WHYTE: Let's just give her it. She's been complaining the whole time.
(Laughter.)
DR. WHYTE: We'll let her have it. Okay. All right.
I know, I know, but -- okay. I'll let Team 1 choose. How's that?
Okay. Fine. Chad wants to enforce the rules.
Team 4?
TEAM 4: Play It Safe for 400.
DR. WHYTE: You're Team 1, but she agrees. Team 4. I don't know. Team 4. Yeah, it's all

about collaboration.
Play It Safe for 400. This is one of the many systems the FDA uses to collect reports on adverse drug events. There are a couple of answers. Team 3?
TEAM 3: Would that be FDA MedWatch? What is the MedWatch?
DR. WHYTE: What is the MedWatch program? That is one of them. Other answers are FAERS, Sentinel. That's correct. Yes.
Team 3?
TEAM 3: Let's do Advocacy Cheat Sheet for 100.
DR. WHYTE: For how much?
TEAM 3: Sorry, for 300.
DR. WHYTE: Three hundred. You're ordering off the menu. This FY, fiscal year, 2013-2017 initiative seeks to gather patient perspectives on their conditions and available treatment therapies in a more systematic way to better inform the drug development and evaluation process.
Team 1?

TEAM 1: What is the PFDD?
DR. WHYTE: What is the PFDD? Yes. That's correct, Patient-Focused Drug Development program. Choose again.
TEAM 1: Play It Safe for 300.
DR. WHYTE: Play It Safe for 300. This phase of the regulatory process occurs after the FDA has approved a drug or biologic product for marketing in the U.S. The FDA monitors these products to detect serious unexpected adverse events and takes action when necessary.
TEAM 1: Phase 4 postmarketing, what is?
DR. WHYTE: Go ahead. You're throwing a couple answers in that.
TEAM 1: What is postmarketing?
DR. WHYTE: You said phase 4. I'll give you that.
TEAM 1: Phase 4.
DR. WHYTE: Go ahead. We'll count that, postmarketing surveillance, but it's often referred to as a phase 4.
Choose again. Everyone can still get in

this, even Team 2.
TEAM 1: Trials and Tribulations for 400.
DR. WHYTE: This landmark legislation, enacted in 2016, builds on the FDA's critical path initiative efforts to foster innovation in the scientific processes for developing manufacturing and evaluating medical products.
Team 2?
TEAM 2: What is FDASIA?
DR. WHYTE: No. That's wrong.
Team 1?
TEAM 1: What is 21st Century Cure?
DR. WHYTE: What is 21st Century Cure? That's correct.
You have gotten it, though, at times, so you can't use that excuse.
Team 1 again. See, I think you're going too much like this. I don't know. Ask Team 1 what they're doing. Team 1 seems to be good at it.
Team 1?
TEAM 1: We'll take Play It Safe for 200.
DR. WHYTE: We're going to clear that up.

These entities are required to report adverse drug events to the FDA. They're required.
Team 1?
TEAM 1: What are pharmaceutical companies?
DR. WHYTE: Yes, or manufacturers, yes. We'll accept that. What is manufacturers, packers, or distributors of products in question?
Yes. Go ahead. Team 1.
TEAM 1: We'll take Acronym Soup for 200.
DR. WHYTE: NME? Team 3?
TEAM 3: What is new molecular entity?
DR. WHYTE: That is correct, Team 3. Very good. We're having a change of players.
Go on. Team 3, choose again.
TEAM 3: Let's do Acronym Soup for 300.
DR. WHYTE: We had a practice, and there were plenty of people that said that, too.
PDFUA. Team 2? Remember, give me all the letters.
TEAM 2: What is the Prescription Drug User Fee Act?
DR. WHYTE: Very good. You don't need the

rest of that.
Team 2, choose again.
TEAM 2: Can we please have Acronym Soup for 400?
DR. WHYTE: Of course you can. Thank you for being so polite. GDUFA.
Team 4? I guess it works, team 4.
TEAM 4: Generic Drug User Fee Act.
DR. WHYTE: Correct. Yes, thank you. Very good. Choose again. Wouldn't that be crazy if you're almost in the lead?
Drugs and Biologics for 400. It clearly works. We hear this on devices all the time. Also known as the prescribing information or package insert, this informative communication provides healthcare professionals the necessary information to appropriately prescribe drugs for safe and effective use. Team 1?
TEAM 1: What is a drug label?
DR. WHYTE: What is the drug label? That's correct. And you are clicking it from the beginning. You maneuvered it well. Very good.

Team 1, go again.
TEAM 1: We'll do Trials and Tribulations for 300.
DR. WHYTE: This entity seeking to market a drug is responsible for its development and proving it is safe and effective.
Team 3?
TEAM 3: What is the sponsor?
DR. WHYTE: What is the sponsor? We'll accept that. It could be drug manufacturer, or distributor, et cetera.
Team 3, choose again. I like your strategies. You click, and then you figure out the answer. That's good.
(Laughter.)
TEAM 3: I looked at the team. Let's do Advocacy Cheat Sheet for 200.
DR. WHYTE: These free public seminars welcome patients, caregivers, and other members of the public to present data, information, or viewpoints on issues pending before the FDA committee.

Team 1?
TEAM 1: What is the drug advisory committee?
DR. WHYTE: What's the answer to that, drug advisory committee? Sure. Let's accept it. What's the answer? Yes, let's see it. Yes. Accept it. I was going to be a stickler. They're sponsored public meetings, but they are similar, so we won't be too harsh. We'll demonstrate agency flexibility.
(Crosstalk.)
TEAM 1: Do Advocacy for 100.
DR. WHYTE: This is one of the many ways patients and advocates can be more involved in the FDA's drug evaluation and approval process.
Team 1?
TEAM 1: The Patient Representative Program.
DR. WHYTE: Okay. That works. Sure. There's multiple ways you heard about them today.
You're right. We did give them a warning, and he insisted I use enforcement discretion. So we're going to give them a negative on that because

they said you didn't answer it in the form of a question, and they said you were given warnings. This is your crowd, but we'll let you choose again. The rules are the rules. I mean, why do we have rules?
TEAM 1: We'll do Trials and Tribulations for 200.
DR. WHYTE: Trials and Tribulations for 200. This phase of clinical trials is typically the final phase before approval and involves human subjects to establish the safety and effectiveness of a drug.
Team 3?
TEAM 3: Wouldn't that be phase 3? What is phase 3?
DR. WHYTE: That is correct. What is phase 3? Very good. See, you learn.
TEAM 3: I'm phrasing the question a little weird.
DR. WHYTE: That's good. Finally, our last couple questions.
Team 3, choose again.

TEAM 3: Yes. Let's do Drugs and Biologics for 200, please.

DR. WHYTE: These drug products are safe and effective for consumers to use without a doctor's prescription. Go ahead.

TEAM 1: What are over-the-counter drugs?

DR. WHYTE: That's correct. What are over-the-counter drugs?

Team 1?

TEAM 1: Drugs and Biologics for 100.

DR. WHYTE: A substance intended for use in diagnosing, curing, mitigating, treating, and preventing a disease.

Team 2?

TEAM 2: What is a medication?

DR. WHYTE: I'm going to say no. Who else? Because medications can be multiple things.

TEAM 3: What is a drug?

DR. WHYTE: What is a drug? That is the correct answer.

Team 3, the last question. Are we having a Jeopardy question, though? Do we have a final

Jeopardy? Okay.

So Trials and Tribulations for 100, this drug evaluation study is designed to answer specific questions and discover if promising new treatments are safe and effective for patients.

Team 1?

TEAM 1: What is a clinical trial?

DR. WHYTE: What is a clinical trial? That is correct. Excellent.

So let's move to our final Jeopardy question. Now, can people bid whatever they want? Is that how it works? Don't people have to put their bids in now or something?

Now you can wager. Team 1, how much are you going to -- are you going to wager at all? Are you all in?

TEAM 1: We're going to go for 100.

DR. WHYTE: Oh my. Okay. Fine. Yes.

Team 2?

TEAM 2: We're betting everything we have.

DR. WHYTE: Good. You wouldn't even be eligible to be in it, but okay, we'll let you play.

Team 3?

TEAM 3: We are all in.

DR. WHYTE: Okay. And Team 4?

TEAM 4: All in.

DR. WHYTE: Team 1, you sure you don't want to bid like $210 or something?

TEAM 1: We'll go 199.

(Laughter.)

DR. WHYTE: Let's see that final question. Remember, I give you the answer -- no. It's supposed to be the other way around. This is a hard one, then.

The number of new molecular entities CDER approved in 2016. This wasn't the question that I was expecting.

(Crosstalk.)

DR. WHYTE: Yes. Yes. It does have to be exact. One second. Can they choose now? Buzz in.

(Crosstalk.)

DR. WHYTE: Let's have team 2 answer first. We'll have everyone answer, and then I'll tell you the right answer.

TEAM 2: Since we have nothing riding on this, what is 13?

DR. WHYTE: Okay. What about Team 1?

TEAM 1: What is 16?

DR. WHYTE: Okay. They're both wrong.

What about Team 3? Team 3?

TEAM 3: Thirteen. What is 13?

DR. WHYTE: Didn't someone else say 13? And I said he was wrong, and you're wrong, too.

(Laughter.)

DR. WHYTE: Team 4, what's the answer?

TEAM 4: Twenty-two.

DR. WHYTE: Twenty-two is correct.

TEAM 4: We got there at the end.

DR. WHYTE: Well, no, because Team 1 only bid 199, so they're still going to be higher

TEAM 1: You only lost by a dollar.

DR. WHYTE: Yes. You only lost by a dollar with a broken clicker and unhappiness. But you all did very good. Clearly, you've learned a lot.

So congratulations to Team 1, who pulled it out. You only lost by a dollar.

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(Applause.)
DR. WHYTE: You did well. You won. Sadly, you can only have one winner in Jeopardy, but you're all winners in our book.
Now we're going to talk a little bit about social media. I'll be honest. We're not always the best at social media, tweeting, and Facebook, et cetera, but we've made tremendous progress, especially in the Office of Communications.
I'm very happy to introduce my colleagues from OCOM, our social media lead, Kim Chiu, as well as Raj Patel, who are going to talk about knowing the moment it happens, CDER's social media program.
Now for Raj, he is from a family of eight pharmacists, so I'm sure there's lots of interesting discussions around the dinner table. And Kim is five months pregnant and expecting her first child. So what can be more fun than that? Until it comes to staying up late and changing diapers.
So they're going to tell us about tweeting, and social media, and all those good things. So

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it's a duo, a powerful duo that's going to speak.
Presentation – Kimberly Chiu
DR. CHIU: Thank you, Dr. Whyte.
As he mentioned, my name is Kimberly Chiu, and I am CDER's social media lead. And with me is my colleague, Dr. Raj Patel. We are here to present on CDER's social media program, which is designed to help the public, including patients, stay informed with the latest drug information.
Now, a quick disclaimer before we begin. Neither one of us have backgrounds in social media. We're actually both pharmacists, healthcare providers who care deeply about patient safety and understand the importance of health communications and education.
Also, being from the communications office, we understand and recognize that the public does not come to FDA's website for their information. So that's why part of our goal for this program is to make sure that we are pushing this information to where our audiences are. And in today's era, that also includes social media.

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It should be noted that patients are by no means the only target population for this program. For example, we also target healthcare providers among our audience, so physicians, nurses, and other pharmacists.
Now, I'm going to turn it over to Dr. Patel, who is going to go into further detail about each of CDER's social media channels.
Presentation- Raj Patel
DR. PATEL: Can everyone hear me okay? Thank you. So as Dr. Chiu mentioned earlier, we're from the Office of Communications, but more specifically, we're from the Division of Drug Information.
The offices consist of the Division of Online Communications, the Division of Health Communications, and the Division of Drug Information or DDI for short.
DDI is the focal point for public inquiries regarding human drug products as well as center initiatives. Our mission is to optimize CDER's education and communication efforts to our global

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community, and we accomplish this by engaging in effective internal and external interactions to provide timely, accurate, and useful information through both our traditional channels as well as our social media channels.
DDI is staffed with a team of pharmacists and other healthcare professionals who answer public inquiries that are received by both telephone, e-mail, social media, as well as traditional mail. So on average, our office responds to over 3700 phone calls, over 1400 e-mails, and about 64 letters each month.
How do we disseminate CDER communications? We utilize several different platforms in order to disseminate information to our stakeholders. We initially began in 2010 with our @fdadruginfo Twitter handle, as well as drug safety communication podcasts.
From there, we've grown to using Facebook as well as LinkedIn and other platforms, which we'll discuss further on in the presentation. Each platform provides us a unique audience to reach and

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to provide timely information to.
We'll first begin with our Twitter page. And just by a show of hands, how many of you follow us on Twitter?
(Show of hands.)
DR. PATEL: Good. I see some hands out there, so I'm happy to hear that. As I previously mentioned, we created our Twitter account in 2010, and we had just a few followers at the time. And from there, we've grown to having more than 224,000 followers.
What's great about Twitter is that it has a 140-character limitation, so this allows you to get short bits of information that you can overview at a glance and then determine if that information is pertinent to you as you scroll through your Twitter feed.
We're also on Facebook, and currently we have 511,000 fans of our Facebook page. One important thing to note about the FDA's Facebook page is that CDER is not the only center within the agency that provides communications on the Facebook

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page, so you'll see communications from each of the centers within the agency.
We're also on Pinterest. The agency's on Pinterest. And what we have is a drug-topic-specific board that provides drug approvals, drug safety communications, as well as drug trial snapshots that we discussed earlier today, and so has more information.
So this provides a visual way to see our communications, and it's managed by our sister division, the Division of Online Communications. So what you can do is you can pin drug topics that are interesting to you, add them to your own personalized board, and this way it's very much individualized to what your needs are.
The agency is also on LinkedIn. We have a LinkedIn page to target professionals, so feel free to follow us on LinkedIn to receive notifications about drug approvals as well as other drug safety information.
In addition to our main FDA LinkedIn page, we have a LinkedIn group specifically for

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pharmacists called the Global Alliance of Drug Information Specialists or GADIS for short. The purpose of this group is really to target pharmacists.
We recognize that pharmacists are an integral component of patient care, so we wanted to provide timely information to this important group of healthcare providers, so we have this special group for them.
We also have another great platform that we use to disseminate information to our stakeholders, our drug information listserv. What's great about the listserv is that you're in control, so you can determine how often you receive communications from us. So you can control whether you receive information on a daily basis, a weekly basis, or a monthly basis.
In addition, we also produce drug safety podcasts. The drug safety podcasts are for healthcare providers so that we can provide them with emerging safety information in conjunction with the release of a drug safety communication.

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And I personally love the podcasts. What I really enjoy about the podcasts is that it gives our stakeholders an ability to be on the go.
So you can listen to these podcasts from a mobile device, your laptop, or an mp3 player. So this allows you to have the flexibility of listening to important communications from the FDA while you're driving to work or at the gym. And our podcasts are available on iTunes, they're available on ReachMD, as well as our FDA webpage.
What is the type of information that we disseminate using these different platforms? We disseminate drug approvals as well as drug safety communications, important drug safety alerts like product recalls, meeting announcements such as this PASE meeting, as well as tainted dietary supplement products, as well as health campaigns and a lot more.
At this time, I want to hand it over back to Dr. Chiu, who will discuss how we engage our stakeholders on social media.
DR. CHIU: Thank you, Raj. So after the

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communication is disseminated through CDER's various social media channels, the Division of Drug Information or DDI will then begin monitoring and responding to comments that we receive through these channels. So during this next half of the presentation, we're going to focus on the social part of social media or engaging with our audiences.

We thought this may be best done through a real-life example to help take you through this timeline of events. And some of you may be familiar with this recent recall with EpiPen and EpiPen Jr.

A little bit of background about this recall, the firm recalled certain lots of EpiPen and EpiPen Jr. after the firm had received reports of two devices failing to activate. Now, this occurred outside of the United States, but out of an abundance of caution, the firm decided to also include lots or batches that were also distributed within the United States.

This communication posted on March 31st, so

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a little over a month ago. And once it posted and was made available online, CDER pushed it through our social media channels. And through these efforts, we were able to reach over 165,000 subscribers of our e-mail listserv. Our tweet made over 12,000 impressions. The Facebook post reached over 365,000 individuals. Then also, on the GADIS LinkedIn group, we were able to reach over 140 members at the time.

So after disseminating this recall notice, we then begin monitoring for the comments and questions from the public. It should be noted, though, that at this time, unfortunately, we only have the resources to engage with our audiences on the Facebook platform, but we are expanding and looking to engage with folks in the near future hopefully on Twitter soon.

So on the Facebook post, we received about 250 comments. Now, the large majority of these comments were actually not directed to the agency. They were folks tagging their friends or family members, making sure that they saw the recall

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notice and making sure that it showed up in their Facebook feed.

Of the comments that the agency did receive, you can see on the slide highlights some of the common themes that we saw. So they were things such as will the firm issue refunds or replacements. Some expressed that they needed help with the recall process. And we also received comments about the general cost of these products in general as well.

So the agency will respond. We will answer questions, and we will address concerns to the best of our ability. One example on the right, we've received a question asking whether or not patients would be responsible for the payment of these replacement recalled products. And we were able to direct them to the firm's commitment to replacing these products free of charge.

We will also address misinformation and mistruths that we find on the Facebook page that we believe challenge our mission to protect the public health's health. So on the left-hand side, you'll

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see an example of an individual that promoted the use of an epinephrine product that's labeled for animal use and as an alternative to these recalled EpiPen and EpiPen Jr. products. So we warned patients not to use products that are not FDA approved for human use and also make sure that they refer to their healthcare provider before using any products.

It's important to remember that social media is only one small part, one cogwheel, of the overall communications landscape. At the Division of Drug Information, we still receive e-mails, phone calls, and even handwritten letters. And we want to make sure that we make ourselves available through the channels that patients and the public want to engage with us on.

We will also engage with the public through social media events. We will host and also participate in social media events, including live tweets and Twitter chats. For live tweets, for those of you who may not have had an opportunity to participate in one, these are when you send tweets

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while an event is occurring, for example an in-person presentation or a meeting. And what's great about live tweets is that it takes an event that may have only been accessible by attending in person and then bringing it to a larger audience that may only be able to participate online.

So here's an example of a recent live tweet event that we did. It was an FDA meeting that discussed the possibility of over-the-counter monograph user fees for industry. This was an all-day FDA meeting, and we tweeted highlights from various speakers' presentations. We also tweeted a picture from the room so that folks online could feel as if they were there or at least get a sense of what the room felt like. And we also monitored for tweets looking for any common concerns or any questions that we could address during the event.

As I mentioned previously, we also host and participate in Twitter chats. Twitter chats are live Twitter events where folks can come together online, and learn and talk about a specific topic, and they do this through an identified hashtag.

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This is a recent Twitter chat that we participated in that was hosted by our colleagues from the Office of Women's Health, and the topic was Safe Medication Use and Other Tips During Pregnancy. So CDER, we were able to support on that safe medication use piece.

That's our presentation. Thank you very much for the opportunity to present on our social media program. We'll take any questions that you may have. And if you would ever like to reach out to us individually, please feel free to do so through our listed e-mail addresses. Thank you.

(Applause.)

Questions and Answers

DR. CHIU: And I see we have one question.

MALE AUDIENCE MEMBER: So I just have a real quick question. Can you give an idea of when you have an event that happens like maybe with the EpiPen example that you gave or something like that, how something like that and then reaction to that can inform you for the next time that something like that happens?

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DR. CHIU: So for the EpiPen, for something like this, sometimes we have advance notice that communication will be coming, so we want to make sure that we get that information out as soon as possible. So our team will actually stay on call, stay through late at night, until the information posts so we can get it out as soon as possible.

Then we begin the monitoring process, and we collect the information, and we report it up to Dr. Woodcock, to the other office directors and say these are some of the questions that we're getting. These are some of the common concerns that we seem to be getting about this specific recall. Is there that we can do?

Sometimes we'll issue follow-up communications, or sometimes we'll reach out to the firm or see if there's something else that needs to be tweaked. But we definitely take those comments that we receive, not just from social media, but through the phones and the other channels that we get, and we definitely use those.

Any other questions?

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DR. WHYTE: That's our Twitter handle. Right? Do you have any other CDER Twitter pages?

DR. CHIU: No. We just have that one Twitter handle.

DR. WHYTE: Good. So follow us on Twitter.

DR. CHIU: Yes, please.

DR. WHYTE: We have to get ahead of Dr. Oz in the Twitterverse.

(Laughter.)

DR. WHYTE: So now, I'm going to introduce you to Shawn Brooks. His fun fact is, when he was a professional football player -- remember Regis and Kathy? He was on Regis and Kathy, he says, defending Shaq O'Neal in a basketball game, but I read what I'm told.

Shawn?

Audience Response Questions

MR. BROOKS: It's the truth, by the way, and good afternoon. So we're on to the next portion for our audience response questions. You have your clickers readily available, and we'll have about 20 seconds to answer each of the questions, statements

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that are presented to you.
Ready? First statement, please rate your level of agreement or disagreement with the following statement. Following the how to get your voice heard presentation, I feel that I have the necessary information and resources to request a meeting with the FDA.
A is strongly agree; B is somewhat agree; C, neutral; D, somewhat disagree; and E, strongly disagree.
(Audience answers.)
MR. BROOKS: It looks like everyone is there. Somewhat agree, very nice and strongly agree, so good showings there. And for the 6 percent that doesn't have it, we're certainly available to discuss and see where you might be feeling like you're not as confident about interacting or engaging with the FDA.
Next question, please. You can engage with the FDA using the following communication channels. A, Facebook; B, Twitter; C, e-mail; D, phone call;, E, postal delivery letter; or F, all of the above.

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(Audience answers.)
MR. BROOKS: Looks like we have 98 percent correct, so it's all of the above. For the Facebook folks, you were partially correct, considering the presentation we just had, but it's all of the above.
(Laughter.)
MR. BROOKS: Next. The status of any drug currently under review is public information, true or false?
(Audience answers.)
MR. BROOKS: Looks like everyone's in. There we go, 67 percent said false, 33 percent said true. The answer is false.
DR. WHYTE: That's an important point, which we talked about earlier. Because it's not public information, we often can't discuss it. That doesn't mean that we're not interested in the issue or we're trying to be obstructive. That actually is the rule of the law.
MR. BROOKS: Drug manufacturers are required to report adverse events from a drug to the FDA. A

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is true; B is false.
(Audience answers.)
MR. BROOKS: And the answer is true, 96 percent. Very nice. So yes, drug companies are required.
Thank you.
(Applause.)
DR. WHYTE: So now, you listened to the FDA since about 9:00 a.m. this morning, we wanted the opportunity to hear from folks that have had a lot of interaction with the FDA and can tell you what their tips are, what their best practices have been in terms of engaging and interacting with the agency.
So it's completely uncensored and unfiltered. They can say what they want. I'm delighted to welcome up to the stage Cynthia Bens, who's the vice-president of public policy for the Alliance for Aging Research.
Now, her fun fact is, she spent six years as a fashion model through high school and college before graduating and starting her career in public

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policy. But what I love about Cynthia, she included an "alternative" fact.
(Laughter.)
DR. WHYTE: But I think it actually is a fact in this setting. And her alternative fact -- and it actually says that -- is that she and her husband have made it a goal to visit all of the countries where their ancestors came from to better understand their heritage. So far, they've visited six countries.
I will tell you, I was in Hamburg, Germany for a DIA Europe meeting, and there's Cynthia Bens in the audience. So I don't know if that was on your circuit at the time, but welcome.
Now, are the two of you going to sit together, or talk independently, or how are you going to do it?
I also want to welcome Jane Larkindale, who's the vice-president of research and development for the Friedreich's Ataxia Research Alliance, and she's been deeply involved in the externally-led PFDDs. You might want to talk about

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that on June 2nd.
Her fun fact is, she's lived in big cities in seven countries, and then finally settled on the edge of Tucson, Arizona with a garden full of cacti, a resident bobcat, a javelina, which Noah and I looked up, and multiple desert creatures. So that's kind of like some big cities, too, in a way.
So the time is yours. Say what you feel comfortable with, but the goal really is for all of you to hear from folks who have engaged fairly regularly and extensively with the agency. And I hope it's been in a good way, but I'll let you speak. Thank you.
Presentation – Cynthia Bens
MS. BENS: Thank you, everyone, for the opportunity to be here. I really think that this is an incredibly important meeting. I know I had the opportunity attend last year as well, and it's very humbling when the FDA recognizes you and your organization as a pro for engaging with CDER.
I can honestly say everything that we've been able to accomplish in working with CDER and

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the disease areas we care about has only been because communication really is a two-way street, and we found that -- I know you had a presentation earlier today called "Have Your Voice Heard," and FDA has made it incredibly easy for us to have our voice heard. But it also takes a lot of work, so I'll walk through some steps with you.
But before I start with the two examples I'm going to give today. I'll give you a bit of background on the Alliance for Aging Research. It was started 30 years ago because there was no organization that existed that was focused on the importance of prioritization of research into the aging process and to apply it in ways that help keep people healthier and more independent longer.
When we initially started out, like a lot of groups that are here, I know we were focused on things like NIH funding for research, and we still very much to this day care about that. But it was about 11 years ago, when we started to look at the pace of application of research in specific disease areas and the problems that were happening with

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actually translating that into interventions for some really challenging diseases of aging.
So the first example I'm going to talk about is work that we've done in the areas of Alzheimer's disease. We looked at Alzheimer's because of the increasing prevalence that was going to be coming, but also because there were a number of companies that were looking to develop treatments for Alzheimer's, and we're having a very tough time actually getting better treatments to market for Alzheimer's.
We were all incredibly frustrated at the time we started the organization, Accelerate Cures and Treatments for Alzheimer's Disease. There were 15 of us. We were all nonprofits, and we wanted to have our voice heard. And we were surprised that there was no single voice that was communicating directly with the Food and Drug Administration on ways to get past the hurdles with clinical trials for Alzheimer's.
So we quickly grew the coalition to 53 nonprofit members is what we have today. We have

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aligned ourselves with a number of experts in Alzheimer's disease, and we are very open about the way that we interact with the drug industry, and I'll talk a bit about that more.
But when we first started, there was no Patient-Focused Drug Development initiative. There was really the Office of Constituent Affairs and Stakeholder Engagement. At the time, it was called OCSE, where we had to start beating on the door with saying that you have had a very proactive response in some disease areas like cancer, and HIV, and AIDS. And we know that Alzheimer's is going to be that big a deal, and we want to make sure that we're doing everything we can as advocates to get to the point of effective treatment.
We were fortunate that one of the first things that the Office of Health and Constituent Affairs did for us was get us a meeting with the commissioner. We went in at the time with our leadership, and it was 10 other groups that now formed the advisory board in the nonprofit, the

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nonprofit side of our advisory board. And we asked for a number of different things because we did our homework and we saw why HIV-AIDS and the cancer community were so successful at getting to the point they were at.

It was a couple things. The first is, there was representation from the patient community on every opportunity, every advisory committee that there could be, and there wasn't a program for there to be a patient and caregiver representative for Alzheimer's.

So we asked for that in our meeting. That was our first ask, would you please set up a patient representative program for Alzheimer's disease? And FDA said, sure. You need to help us get the patients and caregivers. And we were like we can deliver that. So that was success number one.

The second thing we asked for was the ability for the different centers and offices that have a hand in looking at new drugs for Alzheimer's, that they had the ability to, in some

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way, have an informal group where they talked to each other.

We thought it should be more formal. We asked for an office of Alzheimer's, and they said we're not doing that, but they established something called the Neurology Across FDA Working Group. And the great thing about that group is it was actually co-chaired from the start by Bob Temple. So they took it very seriously, and it's active to this day. They talk about ways that they can share expertise on neurology issues, so it's broader than just Alzheimer's.

The last thing that we asked for, for Alzheimer's, was the ability to work with the review divisions on an annual meeting because we know that it's really difficult for people from the review divisions to go to every scientific meeting that's out there for a particular disease.

So they said, sure, we'll work with you on an annual meeting. We're going to be having our 10th one in November. And what we did was we wanted to identify areas where there wasn't just a

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specific problem with one company's drug and one type of trial. We wanted to look at those areas that were really cross-cutting, where all of the companies seemed to have sticking points with looking at the populations of patients with Alzheimer's disease, selecting endpoints, measuring what actually matters to patients, so what would a clinically meaningful benefit actually be to patients. We talk about this in a three-quarter-day meeting, and it's a really robust discussion, and FDA does participate quite a bit.

We even got to the point to where, about halfway through our sessions with FDA, they suggest back topics to us where they see that there's particular sticking points where there's a need for more research, a need for more input from a specific community, and even looking at things like combination therapy.

We don't even have one disease-modifying drug for Alzheimer's yet, and FDA said we think we're going to get to a point with you where there's going to be a need for combinations, and we

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want to start talking about that and how we can actually make that a reality.

So unfortunately, we don't have an approved therapy that's better than the ones that are currently on the market, but we feel like we really have had some success with Alzheimer's in that area and with FDA.

We took our success and working in cognitive impairment in older adults and started looking at physical frailty in the elderly. This is a coalition called Aging in Motion that we started. We're the chair of it. There's 35 nonprofit organizations. As you can see in a similar model, we align ourselves with the scientific experts in a specific disease area.

Then we also work with industry. And what's unique about sarcopenia and functional decline in older adults is it's not just pharmaceuticals. It's actually nutrition interventions, and there's going to be an imaging component as well to diagnosing sarcopenia. So we bring everybody under the tent, and we come up with what our agenda

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should be.
What's been really unique for this coalition is, unlike Alzheimer's disease, where there is a lot of entrenched attitudes about how you approach drug development, it's really a blank slate. We saw that there was 25 years of research into this condition. We were compelled by the numbers of people who would potentially be diagnosed with it and the rates of institutionalization that would come as a result of it. So we really felt that this is something that was ripe for us to play a role in convening folks.
So we've done a couple of different things. The first, we were surprised that sarcopenia in the aging space is a household name, but it wasn't a diagnosed condition yet. So we first had to take on working with the CDC to get a diagnosis code for it, which is a totally new process that took us two years, but we now have one. So it's formally recognized as a condition.
The second thing we noticed is that in clinical trials, there was a real paucity of

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endpoints. While there were a number of tools validated for use in looking at sarcopenia, none of them were at the point where they could be recognized for use as outcome measures.
So naively, we took on the role as the leading organization to start going through the qualification process for functional measures for this disease. I'm sure many of you are familiar with this process. It's fairly long. But it has had a really positive effect in getting the community who recognized ways that you would measure functional impairment from sarcopenia to notice that there's a need to now bring the patient and caregiver voice into the process to understand the tools that are already out there that people want to use as endpoints, are they really measuring what matters most to patients?
So we're the ones that are working with qualitative researchers to actually produce that data, and then if we're successful in making it through the qualification process, like every other tool that's gone through that process, it'll be

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publicly available for everyone to use.
So it's not like any one company will have the benefit of having ownership of the endpoint and people who have just an idea about pursuing a program will be able to use it as well. So we're excited about that.
Then the last thing that we did, we just thought that this was an area where FDA needed to have a bit more understanding of the patient and caregiver experience with the disease. So we just submitted comments like anyone else through the Federal Register notice to have a disease added to the list of 20 that was funded under PDUFA V for a PFDD meeting, and we were really surprised when we made the list.
So we were one of the last meetings, but the meeting was just held on April 6th amidst 9 tornadoes and horrible weather. But FDA did a really bang-up job at reaching out to the patient community and trying to get people to attend the meeting in person. And the docket is actually open, so they've been working to try to get

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additional patient feedback into that process. So we're excited for the voice of the patient report to come out.
I'll go quickly. So why am I telling you all this? I'm just going to go through quickly some of the key lessons that I wish someone had been able to tell me when we first started.
I've been at the organization now for 11 years. The first thing is you really do need to educate yourself in the clinical trials process, and there is absolutely no shortcut around this. People will like to tell you things that you need to know about it, but you really just need to put in the time and understand how it works, particularly for your specific disease area.
The most important thing I think that I can stress is learning what information is actually useful for the regulatory process. I know, as people who care deeply about patients and caregivers, we want to make sure that FDA has the full context of everything that patients and caregivers go through, but there is specific

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information that may be lacking and gaps that you can identify by just understanding more about the clinical trial process.

I never thought that we were going to have to lead an effort to go through qualification of functional endpoints. I'm not a special person. I say this a lot. I'm not a scientist. I'm not a regulatory expert. I have my B.A. degree in political science. But there was a gap, nobody else was doing it, and it was something that was a real hurdle to drug development.

So if you identify that gap and you align yourselves with the right people, you can actually make some significant progress.

I think it's important to reconcile your goals with those of the research community and regulatory industry. The reason I say that is a lot of times, research can tend to just continue on, and on, and on with no end. And if there's any way that you as an advocate can play a role in trying to get where the research can better align with drug development, you can be a really

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important force there.

Then with industry, I put that on there because some of the most meaningful conversations that we've had -- and FDA cannot talk about failed trials. But if you're able to engage with industry in understanding what led to some of the trial failures in your disease area, it's been particularly instructive. Sometimes companies can't talk about it, but many of them can, and people are very willing to do it.

So we've learned a lot about struggles just broadly in the clinical trials process by having conversations with industry, but not doing their bidding for them, just better understanding.

The next thing I'd say is work with advocacy groups in your space, and I think that this is working better. One of the things that I think was challenging was when PFDD was going into the externally-led patient-focused drug development meetings. There were a lot of groups that weren't necessarily coming together to put in proposals for these meetings, but I understand that this is

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happening a lot more. And the more you can align together, the more impactful your meeting is going to be to FDA.

Then I'll say listen when FDA speaks about your disease, the only example I'll give you related to this and why I think it's important to sign up for Facebook, and Twitter, and every blog post, and newsletter you can find, even if it doesn't have patient in the name.

FDA put out a sleeper report about three years ago and targeted drug development, and nothing in the title related to Alzheimer's disease. But if you read the report, it actually pointed to Alzheimer's several times.

No one in the community -- it didn't really register with us until we started looking at it, and it was using Alzheimer's as an example of where there are discrete areas in understanding the biology of the disease, a lack of information about the prognostic value of biomarkers.

It was basically a roadmap for, here's where FDA thinks all your knowledge needs to be gained,

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and it gave us sort of enough material for two meetings to talk through where those challenges were. But nobody would have seen it if I and some of my colleagues weren't on every listserv that FDA has getting a lot of e-mails from you guys.

Then just realize that you have to temper your expectations that successful engagement doesn't always result in a drug approval. I'm here to say that I feel like we've sort of been on a journey with FDA, and they're really poised to sort of be responsive when we do have a drug that's ultimately going to be effective for Alzheimer's and sarcopenia. And I don't think that we would have been in this place if we didn't take this journey with them.

So just know that having a positive dialogue and ongoing interaction with the agency is a win in and of itself.

Then always acknowledge when the FDA has gone above and beyond. Really, I think it's a thankless job to work here. A lot of times, the only thing that you hear in the media is when FDA

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has done something wrong or they've come short, come up short in some area. But they do a lot of incredible things, and I think it's our job as advocates to call attention to that.

So I always put up my hall of fame for engagement because if anybody's boss on this list is watching, they all deserve gold stars for how they've really worked with our organizations, because I've gotten e-mails late in the night from some of the people on this list, and I just think they do an incredible job.

So we thank all of them. But I'll stop and answer any questions anyone has. There's my information. Thank you.

(Applause.)

Presentation – Jane Larkindale

DR. LARKINDALE: First of all, thank you very much to the organizers for inviting me. Like Cynthia, it's really an honor for the Friedreich's Ataxia Research Alliance to be considered an example of working well with the FDA. We certainly try to. We certainly hope to. But it's really

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nice to be recognized as an example of that.

Unlike Cynthia's organization, we present a very small number of patients. Friedreich's ataxia, if you haven't heard of it, is a very rare disease.

Back in 1997, when FARA was formed, our founder, Ron Bartek and Raychel Bartek had a son, Keith, who was 11 who was diagnosed with Friedrich's. And what they found was a whole lot of bad news. It's a disease that affects pretty much everything. It's called ataxia. It certainly isn't ataxia, but it also affects the heart, sight, hearing, causes scoliosis, and a host of other problems.

At the time, there was no treatment, no clinical trials, very little research, and no organization, and Rob and Raychel started there. At the time, they felt there was no help and no hope, but that's certainly changed now. And really, the way that Ron and Raychel set up our foundation, I think has really set the tone for the organization in the field since then.

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FARA was founded based on two principles, research and collaboration. And right from the start, Ron and Raychel said we've got to collaborate with everybody. We've got to pull everybody into our field. We have to work with everyone. We've got to be partners. We're a small disease. We can only work with others.

They pulled in everybody they could think in, all the scientists, the clinicians, they brought new people into the field, all the drug developers. Just like Cynthia's organization, we work with everybody. But right from the start, they also pulled in both NIH and FDA, even though at that point there was no treatment, no thoughts of treatment.

We were going to need to know what the regulations we were going to want later further down the path. There are always gaps in every area. I think of 1997, in Friedreich's, there were an awful lot of gaps, though they had just discovered the gene, which I suppose was one step in the right direction.

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I have a quote here at the bottom that really summarizes Rob's attitude at the time, and I think still our attitude now is, "If you're interested in Friedreich's research and we're not collaborating with you, it means we haven't found you. We will."

I would add that these days, even if you're not interested in Friedreich's research and we think you should be, we'll probably still find you, and we will make you interested in Friedreich's research.

It's a really good field and, as I say, right from the start, we really wanted to bring everybody in, work with everybody, and it's been a great journey.

We focus on partnership, and as Cynthia said, we're focusing on the gaps that we need to fill to move forward. Back about eight years ago, we knew we had no really good clinical endpoints, so FARA pulled together a meeting to discuss clinical endpoints. And at that meeting, we invited FDA, and we had engagement across several

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different groups.
They came. They didn't just sit in the background. They led discussions. They engaged in discussions. They got involved with our community, and relationships were formed. And that really started a long-term relationship. And I would say, since then, I don't know how often we meet with FDA in one form or another. They might say it was too often. I never believed that. But it's been a really good relationship.
It all comes down to respect partnership collaboration. We all want the same thing. We want patients to get better. We want medicines that really work for our patient population. And it's been a great relationship.
So in terms of basic lessons, I think I'm going to repeat a lot of what Cynthia said, but we work under the assumption of partnership. We're not going to FDA and say you need to do this; you need to do this. It's really, what do you need from us and what can we offer to you?
If you need information about our very rare

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disease, we'll find it for you. If there's a gap that you see that you need, we'll figure out how to answer that question because we know our patient community, we know our clinicians, we know the people who are working the space.
We very much work in the pre-competitive space. You very rarely see FARA doing anything for one drug company. We're doing it for everybody because we're a small disease. We know we've got to work together, and fortunately the companies understand that, too.
Secondly, we're very much an organization focused on research, so a lot of our interactions with FDA are going to be based around what data do you need, what data do we have, what can we provide you with to help you make your decision making easier?
This comes back to some of the things Cynthia was talking about, about endpoints, biomarkers, understanding of natural history data. We know that we have holes in this area and we're working very hard to fill them. I'd like to say we

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have all the answers, but I would be lying if I said that.
We also very much recognize the FDA is busy. We're all busy. Let's face it. We would all like to have 48 hours in the day. So we try to engage once we have solid questions that we need answered, solid information we need to give, and engage with people who can specifically answer specific questions we need or we can answer questions that they have for us. So we try and keep a very respectful relationship.
I put this slide up just because in the last year or so, these are some of the meetings we've had with FDA, and it really draws attention to the fact that these are answering very specific questions.
The first one was a very small meeting. We heard from a number of companies that they were getting asked to do something with our mouse models that wasn't very practical with our not-very-good mouse models. So we immediately set up a meeting with the Office of Orphan Product Development. It

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was a small meeting. Our mouse experts went through what our models can and can't do.
I'd love to say we have a perfect model of the disease. We don't. We have nine models, and they're all far from perfect. So it was really a discussion of what we can and can't do with those models. It was a small meeting, very precise.
In January of this year, we're on the verge of beginning our first gene therapies beginning to go into the clinic, and we have many, many interactions with CDER. Through the years, we've had drugs go through CDER. We've never engaged with CBER.
So we had a small meeting with CBER just to talk about what natural history data we have available, what background data we have on endpoints and biomarkers and say, hey, this data is available to you. If you have questions, you can come back to us. If you need to know more about the disease, come back to us. So again, it was a small meeting. It was a focused meeting with a very precise goal in mind.

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The final meeting hasn't happened yet. June 2nd, we're having our externally-led patient-focused drug development meeting. And again in this case, we're doing it with Muscular Dystrophy Association and the National Ataxia Foundation, who are the other two disease groups in the U.S. that cover the ataxias.

It's been a very collaborative process. I have to say that for the very first time, when we sent them the letter of intent and our first communication back from FDA, I have had so much help. Every time I sent an e-mail, I get an answer within 24 hours, however small and piddling a question it is.

It's been a great interaction. We've worked through all the official channels. We've also reached out to our many contacts at FDA, and I think it's going to be very well attended looking at our registration list. I think Katy [ph] was just telling me we have almost 150 people registered now in total, so I think it's going to be a really good meeting.

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It's going to be in the same format as all the internally-led ones. The only difference is it's not going to be on FDA property. We will produce a voice of the patients report at the end of it. It will not be an FDA document; it will be a FARA document. But we hope it will be able to be used in the same way.

I think our patients are really looking forward to being able to explain which of the outcome measures they find most important, which of the things they find in their everyday lives really affect their lives. And I think the drug developers have an interest in being there to hear that, too, and I think it's going to be a great meeting.

So I really thank FDA for the opportunity to have that meeting and for all your help in setting it up because it's not an inconsiderable amount of work. So thank you.

(Applause.)

Questions and Answers

DR. WHYTE: I want to make sure people had an opportunity to ask some questions.

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FEMALE AUDIENCE MEMBER: Hi. I hope this is quick. I just had a question, even though I had a chance to speak a little bit.

From a logistical level, planning an external meeting, I know that earlier today, it was that they are here to help guide us with the questions and things like that. What exactly, time-wise, resource-wise, is an organization who is planning on doing something like that looking at?

DR. LARKINDALE: So in terms of resources, we've obviously got a budget because you've got to pay for the meeting space, and we've got to support travel for a number of the patients and panelists to take part. So in terms of resources, it's quite a lot from that perspective. The rest of it, we've largely done with internal staff.

It's mostly been a lot of time between talking to our panelists, making sure they know what the whole process is. We've had a number of webinars with our community to make sure they know what the whole purpose is, what sort of testimony

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we're going to expect from them, figuring out what questions we want to ask. They are very much based on the ones that have been asked previously, so that actually wasn't so hard.

We've been collecting a lot of preliminary data from our community, sending out surveys, talking to our community members, and such like, and then developing polling questions, finding software, finding technology for webcasting, all of those details.

We're a small staff, so it lands on two or three people to do all of that from designing the polling questions, to analyzing the data, to figuring out what kind of polling software do I want to use. There's only a small number of us, so it begins to be quite a long thing.

FEMALE AUDIENCE MEMBER: For things like polling software, is there a way for those of us who are coming just a little bit after you to steal those ideas beyond reaching out to exactly, like is there a plan for best practices, sharing [indiscernible – off mic].

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DR. LARKINDALE: I'm not aware of anything formal, but certainly, because I've worked in other disease areas previously, I reached out to both my atomic dystrophy and spinal muscular atrophy who had meetings ahead of us, and they gave me all their materials, which we copied nicely.

We're also working with a consultant, James Valentine, who used to be at FDA, and he's very good at passing on materials from previous meetings with information, of course.

By all means, if you're going into this process, feel free to reach out to me. Those other organizations were so great for helping me that I'm perfectly happy to pass that on and help others.

MS. BENS: I'll just add, even though FDA did host the PFDD meeting for sarcopenia, they did work with us on things. They needed us to get a wheelchair-enabled bus for some of the patients because it wasn't in the budget, and they connected us with one of the other groups who had had an FDA-led patient-focused drug development meeting and had a really nice conversation with that group.

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But I would say that another thing that you want to think about in terms of planning for it and the resource intensity is related to making sure that you have a range of patient experience. I think even though it wasn't an Aging in Motion coalition-led effort, we wanted to make sure, to the extent we could, that there was a range of patient experience represented at the meeting.

So we would keep in close contact with FDA about patients that they were hearing from, whether they self-identified, if they needed more patients who were immobile. And unfortunately, we came up short. I mean, it was really difficult to get people who had significant mobility issues to the meeting in person. That's where the webcast function was I think the most useful, and the docket was useful. But we did spend an incredible amount of time working with FDA on making sure that there was a range of patient experience. So that takes time.

DR. LARKINDALE: If I could add to that, we have the same issue, that we have a very diverse

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disease, and we have young children and people who are extremely physically disabled, including people who have severe dysarthria and can't speak very clearly. And we would include a video to be able to represent some of those patients.

We have one speaker of a patient who was recently deceased. You need the voice of everybody. We decided we couldn't really ask young children to speak in that venue, so their parents will speak for them, but you definitely have to think about it.

MS. TAYLOR: Hello. Thank you both so much for sharing your expertise. I really hope that our organization can be up there with you maybe next time. So my name is Emily Taylor. I'm with the Solve ME/CFS Initiative. We were actually the very first disease to have a PFDD, and that was back in 2013.

So my question to you is what's the next step? We got our voice of our patients. How can we convert that into actionable steps for finding solutions?

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DR. LARKINDALE: So I think there are lots and lots of things we could do. You could go in many, many different directions. One of the areas that I'm very interested in is developing outcomes, and biomarkers, and such like. And certainly, if you look at that testimony and say, well, what's most important to my position is X and our outcome measures don't measure that, maybe that's something you might want to look at.

An expected outcome from ours is we know that fatigue is a big issue in our community, and we don't have a good way of measuring it. So if there are things like that, that might come out, it's good guidance as to where to look for future outcome measures.

MS. BENS: Also, it was timely for us to have the patient-focused drug development meeting on sarcopenia when we did because we're just entering into this phase of helping to support the qualitative research for the tool that we're trying to do. And it gave us some insights into ways that people who have the condition, how it's limited

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their life in ways that we're not thinking about.
I mean, when we think of the measures that currently exist, it's things like inability to use the bathroom by yourself, get in and out of a chair. But there were some insights that we got where one of the woman's mobility limitations impacted her ability to volunteer. So she still tried to find ways to volunteer through a phone bank, but she physically couldn't do the active volunteer work that she used to do anymore.
So depending on how we were phrasing questions and the type of research we did, that was actually a really useful insight for us to have, and I think for FDA to know, as they're thinking about a potential conceptualization of a treatment. How does that map back to some of the things that they heard that were anecdotal that patients did experience?
Then I'd also echo the research gaps. I think that's really important. We as advocates can try to convince NIH they need to be spending more money in certain areas. And to the extent that

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there may be research gaps that NIH is lucky enough to be able to fill or groups that we can work with who can fill the research, that's how we're using it.
DR. WHYTE: I think you also want to think, when you engage with the agency, there should be an ask, and it should be explicit. What do you want the agency to do?
So in some ways, when you talk about patient-focused drug development, what is your goal? Is your goal you want to educate reviewers about a disease process? Is it that you want to talk about the need for different endpoints, a specific patient-reported outcome? Is it about drug approval? Is it about drug safety?
This building and this agency can be imposing, both literally and figuratively, and confusing. But in many ways, thinking through what are you going to ask the agency to do and to be explicit about that is very important for effective engagement.
Both of you are very good at that, and I

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want to thank you for taking the time. I know you're both available by e-mail and by phone to talk to all of you because one of the goals is to learn best practices, and there's no one-size-fits-all, and the process is iterative. This is still a very new process for the agency.
Stand up and stretch. I want to introduce my colleague, Dr. Scott Winiecki, to just have some final polling questions. Scott practiced pediatrics for 12 years before he came to the agency, and his fun fact is he likes to photograph birds. So Scott's going to bring us into the home stretch.
Final Poll Questions - Scott Winiecki
DR. WINIECKI: I'm also at the back table, and I'm happy to talk with anybody. I've already answered some questions, or at least attempted to. And I'm happy to stay once the meeting finishes if you don't have a flight and you're not afraid of D.C. traffic on a Friday afternoon.
So three final polling questions. The first one is, how confident are you in understanding the

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functions of CDER, so A not at all;, B, somewhat; and C, very confident?
(Audience answers.)
DR. WINIECKI: It looks like the majority of people said somewhat or very confident. That's good. That's sort of the whole purpose of today's meeting. And if you're in that 2 percent, by all means, stop by the table, and I'll see what I can do to help. I don't have all the answers, but I certainly have some of them.
Our next question, how confident are you in your ability to navigate through and engage with CDER? A, not at all; B, somewhat; C, very.
(Audience answers.)
DR. WINIECKI: I appreciate your honesty in saying somewhat in the majority. I've been at the agency almost eight years. I've been in CDER for almost a year. And figuring out who to call, and who to turn to, and to navigate is not at all an easy task. Even figuring out the acronyms is still a challenge for me some days. And again, I've worked here for almost eight years.

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But even though I moved two buildings from the Center for Biologics to the Center for Drugs, all the acronyms change. So navigating is not easy. Hopefully, what you've heard today has made it somewhat easier and given you some increased confidence.

Our final polling question, would you recommend this workshop to others? A, yes; B, no.

We're also very interested in your feedback because, obviously, the only way we can improve this for the group of people who are doing this next year, whether it's some of the same people in the room or new people, new advocacy organizations, is to learn what to add, what to change.

So by all means, provide us with lots of feedback because we really do use that. I think today you've seen most of the people in Professional Affairs and Stakeholder Engagement, and we're not a huge group. And obviously, we meet together frequently and work on how to develop these things and how to improve them, so we are very interested in your feedback.

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(Audience answers.)

DR. WINIECKI: So we appreciate your very kind response. Thank you so much for listening today, and we're going to wrap up with a few words of wisdom from Dr. John Whyte.

(Applause.)

Words of Wisdom – John Whyte

DR. WHYTE: Thank you. I don't know if they'll be a few words of wisdom because I know people want to get going. But I do want to thank Chad for helping out with Jeopardy and making it happen, as well as the audience response questions.

I want to give special recognition to the many folks of our team. As you know, this is a big effort, this is an important effort, but we wanted to do it. And I want to recognize Rea and Noah particularly, who have done an enormous amount of planning for this, as well as Milena, and Francis, and my assistant Diane, and Scott, and Mary, and Chris, and Dave, and Shawn. We wanted to be here today to introduce ourselves because we want this climate and culture of engagement.

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Last year, I opened with Dr. Woodcock's comments that patients are experts in their own disease. And you think, "Well, that's obvious. Shouldn't folks know that all the time?" And it's really a recognition that we need to talk to the experts in their disease, and we need to engage them. And that's patients. It's caregivers.

So today is not meant to be a single point in time, but really to start a dialogue. So all of our information is available in the handouts. You should feel free to reach out to me or any member of our team. We'll be around for a few more intersection, so if you have questions and you didn't want to ask at a mic, you can feel free to come up and ask us individually, and we look forward to hearing from you.

So safe travels on the Beltway if that's the way you're going.

(Applause.)

(Whereupon, at 2:55 p.m., the meeting was adjourned.)

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