FOOD AND DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

Navigating the Center for Drug Evaluation and Research

What You Should Know for Effective Engagement

Thursday, March 31, 2016

8:40 a.m. to 3:54 p.m.

FDA White Oak Campus

10903 New Hampshire Avenue

The Great Room

Silver Spring, Maryland

Meeting Roster

Cynthia Bens

Alliance for Aging Research

Catherine Chew

Food and Drug Administration

Office of Communications

Brian Hasselbalch

Food and Drug Administration

Office of Policy for Pharmaceutical Quality

Hang Hoang

Food and Drug Administration

Office of the Center Director

Valerie Jensen, RPh

Food and Drug Administration

Office of the Center Director

Karen Mahoney
Food and Drug Administration
Office of Communications

Heidi Marchand
Food and Drug Administration
Office of Health and Constituent Affairs

Richard Moscicki
Food and Drug Administration
Office of the Center Director

Kathryn O'Callaghan
Food and Drug Administration
Office of Science and Strategic Partnerships

Bernadette O'Donoghue
Leukemia & Lymphoma Society

Pujita Vaidya
Food and Drug Administration
Office of Program and Strategic Analysis

Jason Woo

Food and Drug Administration

Office of Generic Drugs

Janet Woodcock

Food and Drug Administration

Office of the Center Director

John Whyte

Food and Drug Administration

Office of the Center Director

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

(8:40 a.m.)

Introduction and Opening Remarks

John Whyte and Janet Woodcock

DR. WHYTE: Good morning, everyone. If everyone can come in and take their seats, we'll go ahead and get started. I know there is an accident on Georgia Avenue, but we do need to kind of get things moving. And we are webcasting this, and it will be available online. So why don't we go ahead and get started.

On behalf of the Center for Drugs, I want to welcome everyone to Navigating the Center for Drug Evaluation and Research: What You Should Know For Effective Engagement.

So we have an action-packed day. I'll give a little housekeeping note in a few minutes, but I want to start with introducing our center director, Dr. Janet Woodcock.

During her 30 years with FDA, she has served in several different capacities in addition to her current position as the CDER director. And

throughout her career, she has helped the agency elevate and transform its approach to medical product safety, personally leading the way on many key safety initiatives, from their beginning to implementation. This includes the Adverse Event Reporting System, the rollout of the Safe Use Initiative, the Sentinel Initiative, as well as establishing, most recently, the Office of Pharmaceutical Quality.

Throughout all of these accomplishments and many others, Dr. Woodcock has helped ensure that the FDA can fulfill its mission effectively. She's championed the use of innovative new tools and approaches and has flourished and enriched many partnerships with industry, academia, health providers, patients, and colleagues across the FDA.

She's a rheumatologist by training. She often says she's a chemist in terms of her thinking. And as some of you know, she's an avid gardener. So if you want to get Dr. Woodcock's attention, just bring up the topic of orchids. That's what I've learned.

As some of you know, I spent nearly a decade at Discovery Channel prior to coming to FDA. I've been here a little over two years, and still, about every month, I get the question, "Why would you ever leave Discovery Channel to come to FDA?" And the answer quite simply is because of Dr. Janet Woodcock.

It has been Dr. Woodcock's vision to create a new culture of engagement with patients, to have true two-way communication, and not just to push information on either side, but to understand each other's perspectives, to educate both groups, the FDA as well as patients, on each other's concerns and interests, and really to try to find a path forward on common ground.

This meeting today would not have happened without the leadership and the vision of Dr. Woodcock. So you don't get a lot of opportunities in life to change a culture. So that's why you leave a place like Discovery Channel to come to the FDA to work with someone like Dr. Janet Woodcock.

So it's my great pleasure to introduce the center director, Dr. Janet Woodcock.

(Applause.)

DR. WOODCOCK: Thanks very much. Thanks, John.

Well, John brings a set of skills that we really need I think at the agency and at CDER as far as that experience in outward engagement. So I really appreciate your being here as well.

Thank all of you for coming, and welcome. Fortunately, we don't have the traditional-like FDA horrible weather, although it sounds like we have a major car accident, but we all have to surmount these things.

We really are happy to kick off meetings where we really explore out engagement with patients and patient groups, and help the patient group figure out how to have the best engagement with the FDA, because it can be challenging, I know.

But the bottom line is, at least for the Center for Drugs, patients are our customers. Our

customers are the people who take medicines, the people who need medicines, the people who care for those who take medicines.

We serve the public. We're public servants. But we're also a production shop. In other words, our part of government, what we do in the Center for Drugs is output, mass quantities of -- we make decisions, we put out labels, we process 1.2 million reports of different adverse events that occur with respect to drugs that are reported to us every year.

We inspect all the facilities that make drugs all around the world. We have about 3,000 meetings a year with those who are seeking to develop new drugs and to help navigate the path to getting onto the market, and so forth and so on.

We have maybe a thousand generic drug applications that we have to process each year, and those generic applications, of course, would lead to generic drugs that would help mitigate the cost of drugs, provide competition, and thus, better access for patients.

So at the end of the day, all of our actions are serving patients. But we have to pay a lot of attention to our production lines and making sure we're moving the freight, and the policies, and the procedures, and the processes are all running smoothly. And it's sort of hard to lift our eyes up, and sometimes our customer service, I think, may not always be world-class as a result, and we probably haven't gotten it right.

Of course, there are about 7,000 diseases out there or more -- there's maybe 10,000 total diseases, so it's really hard for us to encompass all that. Many of the common diseases and even many of the rare diseases, the patient groups and advocacy groups are somewhat splintered and have different points of view, which is fine, but then that multiplies the number of people that we need to interact with.

So my first message to you, if you need to have us do something for you or hear you, which is one of the, I think, focuses of this meeting, get our attention. Hopefully, what you're going to

hear about today is routes of engagement; different ways you can get into the system and talk to the right people, depending on what issue you're trying to deal with and you want us to pay attention to.

In many cases, patients or patient groups have a single issue they'd like us to pay attention to. Now, it might be a side effect that's developed of a drug that they'd like us to investigate.

It might be expanded access to an investigational drug that they would like us to expedite or see if we can't arrange that. It might be a medical error that's occurring with the use of a product that's put on the market that somehow people are making mistakes about.

Whatever it is, that single issue, hopefully, today will help you understand where to go to get that prompt customer service for that issue that you have and get the attention.

For many diseases, particularly diseases that have unmet medical needs, which is a large number of them, where there's no treatment or

treatment isn't very satisfactory, what people seek really is a relationship with the FDA around developing better options for that disease. And I would like to say that the patient voice is really urgently needed here.

We had started this in our last prescription drug, user-fee negotiation three years ago. We had negotiated that we would have 20 patient-focused drug development meetings with patients, and we've been holding those. And I think we've learned a tremendous amount from having those meetings.

One of the things we've learned is, of course, those meetings aren't enough. They're sort of step A, to figure out with the community what are the unmet needs in that disease, what needs to be done, and what is the sort of journey that we're going to have to go on.

But as a follow-up for that, we're going to have to -- we and the drug development community have to respond. We have to have outcome measures that are appropriate. We have to have trials that work for patients. We have to study the symptoms

and other problems that people feel are most important in their disease and not study just the most easily quantifiable thing, because that's what we've always studied, and these are all big changes that have to occur.

I have found, too, that there's another level of patient engagement, which not all of you here, of course, would want to enter into, or would have the ability, because of financial or you have other jobs and so forth, but that is those groups that have really entered in as co-sponsors of drug development or tried to really direct the course of drug development in their disease area.

Those groups that are able to put enough attention into this and raise enough money have literally changed the course of their disease by that type of intense engagement. That involves engagement with the pharmaceutical industry as well, or other drug developers, or intervention developers, as well as the FDA, as well as the academic community.

So that's a really heavy lift, but it can be

done and is being done by some groups. That shouldn't mean, though, that patient groups that don't have the appetite or ability to go that far, that more limited engagement can't be extremely meaningful for you.

So what's being talked about today is a wide variety of things. Some of them are more educational that you can just understand what FDA does in a certain area and maybe make some of our actions more understandable because you realize why we're doing things.

There's going to be more information about the patient-focused drug development meetings and that whole process, and simply an explanation of how the drug development process works. You have a drug developer and their clinical trials, and then you have the FDA.

Most people have a very vague understanding of that, especially all the technical requirements. Patients always ask why does it take so long, why does it cost so much, and there are answers to those questions.

Then, a more recently arising problem that patient groups have had to get involved in and people have been amazed at this problem has been the issue of shortages of drugs, which affects many patient groups, and it's kind of unpredictable who's going to get affected there.

Val Jensen from our shortage group is going to talk to you about that, about how that comes about. It's partly related to some of the issues of some of these wild price increases that we've been seeing for single-source drugs.

Drugs that only are made by one manufacturer and don't have any patent or exclusivity protection are typically vulnerable to either having price rises or the manufacturer suddenly discontinuing. And without any other source, then, there's a shortage. So that's something increasingly patients have become more aware of as that has become more common.

Of course, on the safety side, FDA's done a lot over the last 10 years, and we have a very elaborate structure of monitoring the safety of

drugs both before they get on the market during the trials, and then after they get on the market with both Sentinel, the spontaneous reporting system, and then other studies that we might make the manufacturer do if they're remaining questions that weren't fully answered in the development program.

So science has really enabled us, I think, to put drugs on the market that are much safer in the sense of we understand their side effects -- it doesn't mean they don't have side effects -- but then, say, 30 years ago when we got a lot more surprises after marketing, we have a lot more science to help us understand about drug-drug interactions or liver toxicity and things. We can predict these things much better now. And we have Sentinel and our other postmarket surveillance systems that we can watch and hopefully react very rapidly if an unexpected side effect were to arise.

So I think this day is shaped to try and really orient everyone. I know people are at different levels of understanding because you come from different worlds and have had different levels

of engagement in the past. But I would really like everyone to know that you and the people you represent, the patients, the people who take medicine in this country, really are the customers for the Center for Drugs.

We're here for you, and we are working on a -- I think the PASE group and is really trying to build those bridges so that we can provide you, our customers, with the best access and information possible so we can effectively meet your needs and hear what your issues are in an organized way, and also then respond in an effective way to what those needs might be.

One of the greatest problems we have in this area is this cacophony of voices out there. And often, of course, groups have gone to the Hill, and gone to various parties, so we hear second or third or fourth hand what the needs and problems are. And I think it's far better if we can have an organized way, because we really do try to provide good customer service to all the constituents that we work with and you, our primary people that we

serve, you and who you represent.

So good luck today. I think this is a great idea, getting people to a higher level of sophistication and understanding of all the different processes that go in a center, and what issue you have, how you might come in and get some effective engagement around that issue.

Or if you're really concerned about developing different products for a disease, how you would build that long-term relationship with the agency because that type of effort is a long-term project.

Nevertheless, patient engagement will make a huge difference, I can assure you, in speeding the development of effective treatments for any given disease. Probably patient pressure and engagement and interest are the only things that can really move that along in an effective way. And of course, it's not just on the FDA; it's going to be on the other communities that are involved in researching and developing new treatments and preventive interventions.

So thank you very much. I'm really glad to see all these folk here, and we really look forward to working with you. And I hope the day is educational for you. Thank you.

(Applause.)

DR. WHYTE: Thank you, Dr. Woodcock.

A few housekeeping notes. I've been told to remind everyone to pre-order lunch at the kiosk by registration. You won't be able to use the FDA cafeteria. So please pre-order lunch, if you want to have lunch.

Then hopefully, everyone got a folder when they checked in. It has numerous resources for you, including an organizational chart, an infographic about the drug approval process. All of this information will also be online at our website, where you went to register for the Navigating CDER Workshop. So rest assured, there'll be an opportunity, if you want it all electronically, to be able to receive that.

So it is about engagement. We're going to have opportunities for questions. We're going to

start off with -- everyone should have a clicker in front of them on their table. I know there's also a color card for Jeopardy, and I'm going to talk about that in a little while.

But let's do a couple of test questions that everyone gets comfortable with the clickers. And you should feel a vibration when you actually press your response, so that's how you'll know it'll be working. So don't click it 10 times.

The first question is, is this your first time at the FDA? And we usually give about 10 seconds for people to answer.

(Audience polled.)

DR. WHYTE: All right. Well, great.

The second is, how confident are you in understanding the functions of CDER and FDA: a) is not confident at all; b) is somewhat confident; c) is very confident?

(Audience polled.)

DR. WHYTE: Okay. That's good to know. We have a lot of room for improvement.

Then finally, how comfortable do you feel

about navigating engagement with CDER at FDA?

(Audience polled.)

Presentation – John Whyte

DR. WHYTE: All right. Great. So we have a lot to accomplish today.

Again, before each presentation, I'm going to ask a question, so we'll have use of the clickers. And then after most of the presenters, there will be an opportunity for you to ask questions as well. We'll have some roving mics, and there's also some stationary mics. So if you're shy, we'll come to you.

Real quickly, just a little bit about engagement and how it's evolved over time. As Dr. Woodcock has referenced, it's important to understand how the FDA works, because when you want to know how to engage, in many ways you need to know where to go.

Historically, people would go to members of Congress, people would go to the Office of the Commissioner, partly because they don't know where to go.

I know this is not meant for you to be able to read and there are organizational charts, again, in the folder, but this is just to show you the vastness of the agency. Often people will say, for those that have been here, their first time, this is a huge campus, and many folks will say that the agency regulates 25 cents of every dollar of the economy.

So it can be confusing where to go. This is just the offices at the very senior level, and then this is just CDER. And all the different offices in CDER do not even include every division, et cetera. So again, it is a vast place, and we recognize that it can be confusing as to where do you go and who do you talk to. And even with my own group, there are four different teams.

So today really is trying to, as Dr. Woodcock talked about, create a bridge to patient groups to help you understand where do you go and how do you navigate the Center for Drugs. Because when we think about patient engagement, historically it could be demonstrations and almost

like a mob mentality. And I don't mean that in a pejorative way, but that's really how patient engagement first started, in the setting of HIV.

As this shows, it really has evolved over the past 20, 30 years, where cancer patient advocacy really starting to start in the 90s; and then the first patient representative serving on advisory committee in the very early '90s; and then evolving to voting privileges in the mid-90s; and then having patients as consultants to our medical products, devices, and drugs; and then a health professional liaison program starting nearly 10 years ago; and then really evolving into a patient network; and then ultimately the patient-focused drug development program.

So as you can see, there really has been this trend over time to figure out what's the most effective way for patient engagement, and it's still very much an evolving process.

So again, it's moved from kind of this mob mentality to this individual on one committee representing the patient voice, to more of a

recognition that we need to find a systematic way and an objective way, and a reproducible way, to figure out what is clinically meaningful to patients.

That's really the goal, to understand what is meaningful to patients, because patients are experts in their own disease, so it's important to hear from all of you.

So those are my introductory comments. I'm going to start off with a quiz question for you, so please get your clickers ready. And the first one is -- and it's simple, A, B, C -- most drugs are approved faster in Canada, Europe, or the United States?

Just so you know, I really tried to get music to play for us, but apparently there are licensing issues to get the Jeopardy music.

(Audience polled.)

DR. WHYTE: Well, the answer to the question, and you'll hear about in the next presentation, is the USA, in general. And Hank Hoang will give more statistics. Most drugs are

approved faster in the United States, and that's a common misconception.

So again, I asked that question. You're going to have an opportunity to ask questions very soon.

Before I introduce Hank Hoang, I mentioned I spent a long time at Discovery Channel, and it's hard to be from Discovery Channel and not show video. So I'm going to give you a quick summary of the drug development process through the power of video, and then Hank's going to give you a few more details. So hopefully we can roll the tape.

(Video played.)

DR. WHYTE: All right. So if you know that, you will know much more than most your colleagues. So at this point, I want to introduce Dr. Hank Hoang. Hank is a pharmacist in the Professional Affairs and Stakeholder Engagement Group. He earned his Doctorate of Pharmacy from the University of Charleston, and has been in community pharmacy for several years.

Originally from California, he completed his

undergraduate education at UC San Diego and received a dual Masters of Business Administration and Masters of Finance from Northeastern University.

Now, everyone that is speaking today was supposed to send me a fun fact about themselves. So, Hank's fun fact is he speaks four languages: Mandarin, Cantonese, English, and Spanish, and can play seven musical instruments. So with that, there's no music, but Dr. Hank Hoang.

(Applause.)

Presentation – Hang Hoang

DR. HOANG: Thank you, Dr. Whyte, and thank you all for coming today.

Today, I am going to provide a very high-level overview of the drug approval process. And while there's a lot of steps involved in the drug approval process, it enters the FDA's purview as an NDA or a new drug application. Let's go ahead, and we'll take a look and see exactly what happens when an NDA reaches the FDA and really how the drug approval process works.

In order to understand the drug approval process, we'll have to visit some key objectives. For example, what exactly are the statutory requirements for drug approval, and what's the typical time frame for drug discovery and drug approval, and how much of those time frames are actually occupied by the FDA?

What are the different approval tracks that could potentially expedite a drug's approval? And finally, we'll visit expanded access and understand exactly what it is and how it works.

There's a lot of history behind FDA and the drug approval process and why it was established. But ultimately, all that history really brings us to CDER's mission, which is to promote and protect the public health.

CDER accomplishes this by ensuring the availability of safe and effective drugs, by promoting the safe use of these effective drugs, and really to ensure the quality and the integrity of these drugs on the market.

If we take the drug development process and

really group them into six different stages, we can kind of divide into the following stages, which is providing a little framework first and looking at high level, we'll start with the preclinical stage.

Here researchers must first discover the drugs, and then after testing and test tubes done in animals, they submit something called an IND or an investigational new drug application. The drug can then be tested in clinical studies in humans, and then all that data is compiled into another application called the NDA or new drug application. Here, the FDA actually enters in, reviews the NDA, and ultimately comes to a decision called the FDA action.

All right. Now we have the six stages. Let's provide a little bit of a time frame to this whole process and really see where FDA falls into this drug discovery process.

If you take a look at this blue section, we'll see that drug discovery and the preclinical stage really takes about three to six years, and sometimes the scientists have to go back to the

drawing board because they can't find a drug or isolate a compound. But if they do find one, we can move on to the clinical trials.

Here we can see it typically takes up the majority of the time, because some studies may require the recruitment of thousands of patients, and because of this the clinical phase can really take several years.

Once clinical trials are completed, we'll see in green here, the FDA receives and reviews the NDA and really sets a target action date for within 12 months. And, of course, after approval is granted, there's some logistics like manufacturing, scaling up, and distribution that have to occur before patients are able to gain access to safe and effective drugs.

Finally, the postmarketing phase can occur after approval, and the timeline doesn't stop because sponsors may be required to enter something called postmarketing surveillance.

All right. Let's go ahead and take a deep dive into the first stage, which is the preclinical

stage. Here, the sponsors, which are research institutions or drug companies, are really the ones responsible for developing a drug. The FDA is not the one responsible for developing drugs.

These sponsors have to show the results in test tubes and in animals, and then they have to propose what they want to do in animal testing. Once they compile all these preclinical results, they compile it into something called the IND, the investigational new drug application.

Drug studies can only begin in humans after an IND is reviewed by a local review board called the Institutional Review Board or an IRB for short. The IRB and the FDA really review and outline and approve the protocols of the IND, including objectives such as tests and the procedures of the medications and the dosages, and the length of the study, and other objectives and details of the clinical trial.

The IRBs really have to make sure that the study is acceptable, that patients are informed and have given full consent, and are informed of their

risks. And the researchers have to take the appropriate steps necessary to ensure to protect the patients from harm.

The FDA also reviews the IND application and ensures that the clinical trials won't place human subjects in unnecessary, unreasonable risk of harm. If the IND is approved, ultimately we can move on to the clinical studies.

There are typically three phases of clinical studies. Here in phase 1, it emphasizes safety. Phase 1 usually involves about 20 to 80 healthy volunteers. The goal in phase 1 studies is to determine the drug's most frequent side effects, how the drug is metabolized in the human body, and how it's excreted from the human body.

If phase 1 studies are successful and don't show any unacceptable toxicity, we can move on to phase 2. In phase 2 clinical trials, the drug trials will emphasize effectiveness. Remember, phase 1 emphasizes safety, phase 2 then moves on to effectiveness, and the goal of phase 2 is to obtain preliminary data on whether the drug works in

people with certain diseases and certain conditions.

In these clinical trials, the patients receive drugs compared to other patients, similar patients, receiving different types of treatments, whether it's a placebo or sometimes it could be receiving a different type of drug. Safety continues to be monitored, and short-term side effects are still studied.

Typically, in a phase 2 trial, the number of subjects range from a few dozen to a couple hundred. And at the end of phase 2 trials, the FDA will meet with sponsors to discuss how the larger scale phase 3 trials will begin.

Phase 3 trials can begin to gather more information about safety and more information about effectiveness. This is the phase where trials can focus on studying different populations, and studying different dosages, and using the drug in combinations with other drugs. Phase 3 is usually the largest phase of clinical trials, and the number of subjects can range from several hundred

to upwards of thousands of patients.

As we all know, every person is different. So too is every disease and is every drug. So it's also important to have different approaches to conducting clinical studies. A pivotal trial represents the most important data the FDA uses to determine whether or not to approve a drug. And although most drug approvals involve an average of two pivotal trials, FDA tries to avoid a one size, rigid, fits all approach.

The variation and approach to clinical studies really demonstrates FDA's innovativeness and flexibility in the drug development cycle. The FDA works closely with sponsors to design really what the best approach is to reflect the disease, the drug itself, the patients it's intended to treat, or if other treatment options are even available.

Some factors to consider include whether a drug treats a rare or serious disease or addresses an unmet medical need. For example, we'll take Corlanor here on the left. Corlanor was approved

this last year for chronic heart failure. It was approved to reduce the risk of hospitalization of patients for worsening heart failure and was actually approved with three clinical trials and 667 sites worldwide in over 6500 patients.

Let's take Xuriden on the other hand, which was approved for a very rare inherited disease called hereditary orotic adicuria. In this disease, the body couldn't make uridine, which is necessary for life. Xuriden was approved in a single arm, open label trial after it was conducted in only four patients.

This shows while some trials can require a large number of patients to demonstrate a drug's effects, it may not be feasible or practical in other disease states. No matter what clinical trial design is chosen, the agency always applies the same statutory standards of safety and effectiveness to all drugs seeking approval.

After clinical trials are done, the sponsor will usually meet with the FDA prior to submitting the NDA, and then the NDA will compile all the

information of animal data, of human data, the analyses of the data, and all that science information like how a drug behaves in a body, and even how the drug will actually be manufactured.

Once the FDA receives the application, we have 60 days to determine whether the NDA contains all the necessary sections and studies. And if the application is complete, the FDA review team is assigned to evaluate the safety and effectiveness of the research.

Here we'll take a closer look at exactly what happens to an NDA here at the FDA. It may be a little busy, but we'll break it down. We can see that some FDA reviewers can be involved earlier in the process with pre-submission activity seen as step 1.

The official review time is the time it takes to review a new drug application and issue an action letter outlined in steps 2 to 5. Once an NDA is filed or deemed complete, the FDA review team of scientists, including doctors, including chemists, statisticians, biologists, and

pharmacologists, and other experts evaluate the studies.

Ultimately, this review team is responsible for determining whether or not a drug is safe and effective for its proposed use. The team analyzes these results by looking for possible weaknesses in the study design or weaknesses in analyses, and each reviewer is then responsible for writing up an evaluation and a recommendation and conclusion on the application.

These evaluations are then considered by team leaders, division directors, and office directors, depending on the type of application. And during this time, the FDA sometimes calls on what some of you hear as advisory committees who provide FDA with independent opinions and recommendations from outside experts on applications on marketing the new drug and sometimes on FDA policies.

Whether an advisory committee is called, however, really depends on several considerations such as whether a drug is first in class, or if

it's first for a given indication, or it can raise significant questions or concerns.

Generally, the FDA does take the advice of advisory committees, but it's important to remember that the primary role of advisory committees is just that, to advise the agency. FDA expects to review and act on at least 90 percent of the standard NDAs within 10 months.

Here in red, we can see priority applications, which we'll touch upon in a second, but FDA tries to act upon these with a target date of eight months or shorter.

The FDA also inspects the facilities during this approval cycle, and sometimes manufacturing issues are actually some of the reasons a drug approval may be delayed or denied. That means drugs manufactured have to meet a certain standard, and if a facility isn't ready for inspection, approval can be delayed. Then, we have to make sure that all manufacturing deficiencies are corrected before approval is granted.

So we'll move on to the FDA action stage.

Here, if FDA decides that the benefits outweigh the risks of a drug, they will receive an approval letter and can market their drug in the U.S. But if there's a problem with an NDA or if more information is needed, the FDA may issue something called a complete response letter.

Complete response letters to the sponsors usually address issues such as unexpected safety issues, or the failure to demonstrate effectiveness, or any other issues that really may pop up.

Sometimes a sponsor may need to conduct additional studies, whether it's studies in more people or studies in different types of people, or sometimes they need to conduct a study for a longer period of time.

Sometimes a sponsor is getting ready to scale up and produce, but loses a supplier and ends up with a quality control issue, and that can result in different drug chemistry. We have to make sure that sponsors are able to show that the product on the market will be the same product

tested in research.

Sometimes though, it's a combination of all these products. But close communication with the FDA early in the drug development really reduces the chance of needing to go through more than one cycle of review, but of course, it's not a guarantee.

The FDA's complete response letter outlines the reasons for its decisions and really gives the sponsor a chance to meet and discuss. The sponsor can then ask for a hearing or correct the deficiencies, submit new information, or sometimes the sponsor will withdraw the application entirely.

Even after approval, FDA can still sometimes require sponsors to conduct a postmarket study. The FDA uses these studies to gather additional information about a drug's safety, about a drug's effectiveness, and really the best way to use it. Because it's not possible to predict all the drug's side effects during clinical trials, monitoring safety issues is crucial after a drug gets to the market.

The role of FDA's postmarketing system is to detect serious adverse events and take definitive action when it's necessary. Sentinel, for example, is a national electronics system that enhances FDA's ability to track the safety of drugs once they reach the market.

The Sentinel Initiative really aims to develop and implement a proactive system that will complement existing electronic systems the agency has in place to track adverse events. Sentinel enables FDA to search healthcare data like your EHR, electronic health records, insurance claims databases, and other health registries to evaluate possible drug safety issues quickly and securely.

Another example is MedWatch. MedWatch is a way for the public to report adverse events and other serious safety issues that may arise. These types of programs really help the FDA collect information and really use it to promote and protect the health of the public.

So let's talk about drug approvals. How many drugs do you think FDA approves in a year?

Raise your hand if you think about 10 drugs.

(Show of hands.)

DR. HOANG: Anyone think we approve around 50 drugs?

(Show of hands.)

DR. HOANG: Okay. What about hundreds of drugs a year?

(Show of hands.)

DR. HOANG: Wow, interesting.

Some people think that FDA approves hundreds of drugs a year. Some people think we hardly approve any. But this figure actually illustrates the number of approvals over the last decade.

In 2015, FDA approved 45 new drugs. Of these new drugs, FDA met the target date of approval within 96 percent of the time; 36 percent of the drugs were actually first kind in their class, and over just about half, about 47 percent, were actually approved for rare or orphan diseases.

Now, we saw a little bit on the video and the quiz question, but people often say that drugs being developed are made available to patients in

other countries, such as the EU, perhaps, before they're approved here in the U.S.

Well, here is a graph of four different countries and the percentage of drugs approved the first in that country. The higher the percentage, the more new drugs that were first launched in that corresponding country.

Which color line do you think represents the U.S.?

(Audience polled.)

DR. HOANG: That's right. The U.S. is actually the green line. The FDA of the United States of America actually approves drugs faster than all other developed nations. That's 40 days faster than Japan, 70 days faster than Canada, and 174 days faster than the EU.

What's interesting, if you take all the new drugs that were approved by Japan, by the EU, by Canada, Australia, Switzerland, and the FDA, between the time of 2004 and 2013, over 75 percent of the drugs were first approved by the U.S.

All right. Let's talk some approval tracks

that could potentially expedite the drug approval process, because speeding the availability of drugs that treat serious diseases are really in everyone's best interest, especially when the drugs are first available treatment or if the drug has an advantage over existing treatment.

The FDA has developed four distinct and successful approaches to making drugs available as rapidly as possible. Because all of these actually imply speed, there can be a little bit of confusion about the distinctions and the specific meanings of each, so we'll go ahead and take a look at the first one.

Fast Track. Fast Track is designed to facilitate the development and expedite the review of drugs to treat serious diseases or fill an unmet medical need. The purpose is to get important new drugs to the patients earlier by addressing a broad array of serious conditions.

Breakthrough therapy is the next one and is designed to expedite the development and review of a drug, which is intended to treat a serious

condition or if preliminary data indicate substantial improvement over existing therapy.

The next one is Accelerated Approval. Accelerated approval allows drugs for serious conditions that fill an unmet need to be approved, based on a surrogate endpoint, which is a biomarker used to substitute a clinical endpoint.

Finally, we have Priority Review. Priority review designation means FDA's goal is to take action on an application within 6 months instead of the standard 10 months.

So what does 96 percent of the target date actually mean in months? This chart actually illustrates the average review time for an application over the last decade. The lower the number, the faster the average approval time.

Remember, the average number of new drugs approved increased in 2015, but the average time of application approval was still below the highs of the past.

Lastly, we'll talk about Expanded Access. Expanded access really provides a pathway for

patients to gain access to investigational new drugs. These investigational new drugs have not yet been approved by the FDA, and therefore, they have not yet been proven safe or effective. They may be effective in treating, a treatment, or they may not be.

It's important to remember that there may be unexpected serious side effects that patients really need to consider and all the possible risks when seeking expanded access to a drug. In order to request expanded access, patients will need a licensed physician who is willing to oversee the treatment, to work with the manufacturer, and work with the FDA, to obtain the drugs, to monitor the patient during treatment, and file all the necessary paperwork.

The FDA considers factors on the patients, whether they have a serious or immediately life-threatening disease, and whether there is no comparable alternative on the market, and really whether the benefits outweigh the risks.

Beyond the scope of the patient, the FDA

also must consider if providing the drug will interfere with clinical studies. It could interfere with the completion or the initiation of a clinical study that could support a drug's approval.

Even though a patient may meet the qualifications, your physician may not be comfortable to seek access because of a patient's unique medical history or a unique medical risk, or the physician may not be willing to manage an investigational new drug.

Sometimes the company or the sponsor may not be willing to provide access to their drugs outside of clinical studies or they may not have enough of the drug available for all the expanded access requests.

For those patients who do meet the requirements, however, the FDA generally does approve expanded access requests. Here, we can see the little slivers of green represent less than the 1 percent of requests that were not allowed to proceed. Remember though, only your physician is

the one that requests expanded access, and individual patients are not the ones to apply.

Now, for those of you who want to reference a particular stage or step back and look at the drug approval process as a whole, there are several resources that Dr. Whyte mentioned in the folders available, and we even have the video that Dr. Whyte showed available online.

I want to thank you all for your time and attention.

(Applause.)

DR. WHYTE: All right. So get your clickers ready. A true or false question. True or false, the status of a drug during the approval process is public information, meaning that we can talk about where things are about a drug while it's currently under review.

Is that public information or not public information? So the status of a drug during the approval process is public information. True or false?

(Audience polled.)

DR. WHYTE: Okay. So the correct answer is false. So now we're going to talk about what are the rules of engagement? Because it's important to engage, as Dr. Woodcock talked about, but there might be conditions and circumstances under which we cannot discuss certain items.

So Dr. Rich Moscicki is going to give us guidance in terms of what those rules of engagement are. Dr. Moscicki is the deputy center director for Science Operations at FDA. He joined the FDA in April of 2013, and he's responsible for executive direction of the center operations and leadership and overseeing the development, implementation, and direction of CDER's program.

Prior to CDER, he served as senior vice president and head of clinical development and chief medical officer at Genzyme. He joined Genzyme in the early 90s, and over two decades was responsible for worldwide global regulatory and pharmacovigilance matters, as well as aspects of clinical research and medical affairs for the company.

He received his medical degree from Northwestern University. He's board certified in internal medicine, diagnostic and laboratory immunology, as well as allergy and immunology. He completed his residency in internal medicine, followed by a fellowship at Mass General, and he remained on the staff at MGH, as well as served on the faculty of Harvard Medical School up until 2013.

Rich's fun fact I'm told is he races sailboats in his free time and has participated in several regattas. So with that, Dr. Richard Moscicki.

(Applause.)

Presentation – Richard Moscicki

DR. MOSCICKI: Thanks, John. Listening to all that makes me feel very old.

So my job this morning is to tell you some things that you want to know, but probably also some things you may not want to know, and to really go into some of those issues around the limits of our ability to engage.

But first, let's start with some of the things you really want to know, and that's where are the opportunities for engagement? This has changed over the 20-plus years that I've been involved in drug development.

Early on when I was at Genzyme and sat across the table from my FDA colleagues, I would say to them, "You know, you really got to talk to a patient. You really do." And they would say, "No, no. That might emotionally bias us. We really just have to focus on the science here."

But that's changed, and I'm very happy to tell you that's changed. And you'll see from what you heard before, of a long process that brought that change about, but you can see also on this slide, the multiple different opportunities for FDA to engage with patients.

Now, the one that's turning out to be perhaps the most effective and best way have been these patient-focused drug development meetings. And you're going to get a whole separate talk on that, so I'm not going to go into that.

But there are also advisory committees that you just heard about, and most of these advisory committees do have a patient representative assigned to the advisory committee to present that point of view. But often these patients don't necessarily even have the disease that might be under review by that advisory committee at the time.

We also have public speaking sessions where many patients often take advantage and come and speak, but they often get about five minutes to make their point of view to that advisory committee; that's five minutes each.

Then there are citizen's petitions. Many patient advocacy organizations have the sophistication to submit to us a citizen's petition, which outlines a desired action that they would like us to consider or a point of view for us to consider. So we carefully review those. They often have a lot of legalistic aspects to them.

Then finally, we do put out notices in the Federal Register so that the public can be aware of

some of the things we're doing such as guidances. We do carefully review all the comments, sometimes thousands of comments, that come to us from those Federal Register notices, often from patients and patient advocacy organizations.

Then we often encounter patient advocacy organizations at external meetings. For example, we have an annual meeting that we do together with NORD, the National Organization of Rare Diseases. And there, we often have very lively engagement conversations with the patients and the patient community.

Sometimes patient advocacy organizations request to speak with us on an ad hoc basis and will actually come in, and we will talk to them and engage with them and listen to their points of view.

I think one of the most interesting recent developments for patient engagement has been in the development of guidance. The Duchenne's muscular dystrophy community got together and put together a proposed guidance that they then submitted to us

and which we then reviewed and used as the basis of our own guidance on the development of drugs for Duchenne's muscular dystrophy.

Now, there are also -- or we often receive a lot of emails and letters, and sometimes certain advocacy organizations seem to think that the most effective way is to bombard us with thousands of emails. And while certainly it does get our attention, I can tell you it's probably not the most effective way to be able to get your points across to us.

Maybe the other tough part of this, because, you know, we do want to be transparent. We do want to have dialogue. But often our dialogue is constrained, and it's very uncomfortable for us because we really want to be able to talk back, but we can't, and that's predominantly because of the law.

So we do operate under a strict set of laws regarding confidentiality, and that governs our knowledge of what's going on, our opinions particularly, and what we've been saying to and fro

with a sponsor of a drug that's under development, because that's a very confidential relationship that we have with the sponsor during this period of time.

So that really restricts our ability often to discuss specific products that are under review or in development during that period of time. And I know sometimes it frustrates the patient community that we can't directly tell them what we're thinking or what we think needs to happen next, or what we even think of what we've seen so far.

But the whole reason is that this is really designed to protect the sponsors, and this is congressional action and law, and it's to protect their commercially sensitive information. I mean, you can imagine if we sort of told you what we were thinking, and your brother-in-law was a stock broker, and you at dinner mentioned what FDA is thinking to the stockbroker, and then he went out -- that would be a real problem, and you can immediately sort of see how that could happen.

Now, the other area that I need to talk about is bias, fairness, and consistency. We really do try to be consistent in our approaches, and it's hard because we have a pretty large organization made up of thousands of people, but we work hard to be consistent in that approach.

We also have to avoid showing bias to one company over another. Rather, we have to focus on the scientific facts that are presented to us by one sponsor versus another. And we do actively think hard about making sure that we are acting in that way.

Now, the same thing applies to our work with patient organizations. So we try to incorporate and dialogue broadly with the patients and the industry, and then not just sort of pick out one group over another group.

Sometimes patient advocacy is fractured; shocking information. But sometimes even within small disease groups, we find that there are patient advocates who have one strong view versus another group of patient advocates that have

another strong view, and we have to be very careful to listen to both views and to try and incorporate those views into our thoughts.

Then finally, in the area of bias, I have to say that when people show up on our doorstep being paid for by a sponsor, or if they come to a sponsor meeting and we know that they've been paid for and selected by the sponsor to present their viewpoints to us, we're aware. So we also calculate that into what we hear when we know it's been a very selected point of view that we may be hearing.

Then as much as we listen, as much as we want to incorporate, and I think you'll hear a lot more detail as we talk about the patient-focused meetings, we really do value what we hear. But we can't always follow what we hear, and we don't always follow. We have to act still in an independent manner. And part of that can be due to the fact that the law may not allow us to do what you're recommending us to do.

You'd be surprised. We even get phone calls from Congress sometimes telling us to do things,

and we say, "Gee, I don't think that's legal." And so we sometimes can't always do that.

We may also have a real difference of opinion on the interpretation of the underlying facts. You may or may not be aware, but in fact if you look at the medical and scientific published literature, less than half of it can be reproduced.

So you can't always believe everything you read, even in a medical journal. It doesn't always turn out to be quite the truth. And FDA is the only regulatory organization in the world that looks at the actual data.

For example, in Europe they often will just look at summarizations that were given to them by the sponsor. Here we say, in God we trust, everyone else bring us the data, and we're going to take a very good look at it.

So we may have differences in views on the practicality of the recommendations that are made to us, or as I mentioned before, conflict with the laws or regulations, maybe not in a way that makes it illegal, but which introduces a very significant

legal risk.

Finally, the last two, there can be an inconsistency with the recommendation in our entire policy position or previous decisions. Now, that doesn't mean that we can't change our policy. It doesn't mean we can't diverge from our previous decisions, but we cannot do that lightly, because that would not be fair or consistent. So when we do make a change, it has to be very, very carefully considered and well supported.

Then finally, there's often an evolution of underlying data. So what does that really mean? It means that sometimes the information that we get recommendations from, we know is based on older information, and that because we work with sponsors across an entire area, we're often aware of information that isn't public yet that may influence us in how we make those decisions.

Bottom line, though, I don't want all that to discourage us here today. We really do want to engage. I just wanted to be sure that you knew the rules that we have to operate under as we do that

engagement. Thank you very much.

(Applause.)

DR. WHYTE: Dr. Moscicki is available to take a few questions. We also have about a hundred people online, so, Dr. Green, you can let us know if anyone submits a question. For the folks that are watching it online, there's I believe a text box that you can type your question in. That'll come to us, and then Dr. Green will ask it.

So if you have any questions, you can either come to the mic or raise your hand, and as I said, Dr. Moscicki has a few minutes to answer some questions.

MS. BARNES: Hi. My name is Teresa Barnes. I'm a patient advocate for a number of lung diseases mainly in fibrotic disease. It seems that -- I know FDA continues to evolve and has evolved for most of its existence. And it seems that -- I mean, I realize FDA is currently a guidance organization and primarily provides guidance for industry and so forth. But if you're a patient advocate -- think of us, most of us in

the room are probably advocates, so we're sort of at the mercy of the FDA and industry.

So we're over here going pick us, develop something for us. The problem is, for a lot of these diseases, that's not happening or it's not happening at a level that's really going to change outcomes in the near future. But FDA is sort of this omnipotent being.

So FDA sees what's coming in the future, and it knows who the sponsors are -- not even who they are. Who cares? We don't care who they are early on. We care what they are, what they're working on, what might matter to our diseases. So we can't know the future like you can.

So FDA knows that in the future for these diseases there are things in the pipeline that could affect those diseases. And really, other than the individual companies that are involved, FDA's the only entity that knows that.

So it seems like FDA has a bit of an obligation potentially, as a thought, that maybe it could flag holes and say, okay, we can't tell you

who these people are. We're not going to be that transparent. We can't tell you exactly what the drugs are and exactly what these drugs may do, but we can tell you where these gaps are, and we can say, okay, these set of diseases are going to have potential options in the next seven or eight years, or these absolutely probably won't.

So we can look often like the Office of Rare Disease here does, and identify gaps and look for ways to fill those, rather than waiting until we all figure out, oh, there's nothing in the pipeline.

DR. MOSCICKI: Right. So let me respond in a few different ways. So one is, I hate to tell you, but we're not omnipotent.

(Laughter.)

DR. MOSCICKI: Yes, it's true; we are not. And in fact, I know that there's this sense that we can do whatever we want, but my whole point before is we can't. We're governed very strictly by laws set by Congress that limit our capabilities to do certain things or to talk about certain things.

So that puts a crimp on the kinds of things we can do or the kinds of things that we might even be able to reveal to the public.

I think that we do take our -- we sort of play a role of shepherds to drug development, and that's where our guidances come from. The guidances are designed to let people know, particularly sponsors, what we're thinking. So if you come to us and you did what's in our guidance, you'll probably make us feel like you've done the right thing in developing something for that drug or disease.

Often, we pick a disease that we will actually offer guidance on developing drugs for that disease in order to facilitate development of drugs for that disease. So I think that patient advocacy organizations can often engage us on their desire to see guidance put forward in an area.

But the number one and two things that I think end up really limiting development of drugs for certain diseases is the science and the money, and unfortunately we don't do that. So when the

science is there, even for a rare disease, even for a rare disease in which sometimes there's 12 patients in America, companies will develop it because the science is there, and they can do it.

You can't take -- that genie comes out of the bottle, and sometimes investors will then put money forward to allow those companies to develop those.

Now, we do try to encourage -- not just with guidance in certain areas, but for example, antibiotics for resistant bacteria, we see this as a terrible threat to America. So we've been working very hard to look at all of our guidances to make them as facilitative to sponsors and to encourage them to engage and develop antibiotics for areas like this.

I come from rare disease development. When I was at Genzyme, most of the drugs that we were developing were in the area of rare diseases, and so my heart and soul are still very much in the rare disease area.

We do want to work with the rare disease

community. We can think about how we might be able to do something, like what you say, within the confines of the confidentiality laws that we have to work under.

DR. ROBERDS: Thanks. I'm Steve Roberds. I'm with the Tuberous Sclerosis Alliance. I have a question and it's also related to rare diseases and kind of a gap I see in patient engagement. So maybe you can help me see if we can fill in the gap.

That's around the conversations on endpoints or enrollment criteria particularly for phase 3 or for phase 2 studies, where the patient voice of what's realistic and what's the true unmet need, and what endpoints are important, is difficult to get, based on what I just heard.

Because I heard that while there are patient representatives that can come to meetings from the FDA, they probably don't have that disease, and in the case of rare diseases, they probably haven't heard of that disease.

Then I heard that sponsors, of course, can

bring whomever they want, but if they're bringing patient advocates, FDA has to look at that with sort of a critical eye, but FDA is prohibited from talking to the advocates for that disease directly because of the confidentiality.

So I can't figure how that conversation -- I think it's a valuable point of view, but how do we get that so that we can communicate that in an unbiased way to FDA from the patient point of view.

DR. MOSCICKI: Right. So I think that's part of what our patient-focused drug development meetings were designed to do, was to get that unbiased viewpoint from patient communities about what are the important endpoints; what are their risk tolerances; what's their tolerance for uncertainty? In terms of the amount of information that we might have at the time we would approve a drug, how does this disease impact them? And how do current therapies really benefit them or not?

So that's a great way, but it's inadequate, and we're the first to say that because it's not going to cover all the diseases. You're going to

hear more about it, so I don't want to steal all that thunder. But clearly, the next step is for us to develop and help develop the science of patient input. That's a really critical issue for us as we move forward.

So really being able to get unbiased patient input on those important elements, whether it's surveys or whether it's questionnaires, and patient advocacy organizations can play a huge role in this. And they could even sponsor their own patient meetings and invite us to come.

So there are a lot of ways we can do this I think. I will say, we do also have special government employees, that sometimes we take patients and we will bring them in and listen to them. But the buddy system isn't the best way to do it in terms of getting that patient input. We've sort of learned. And it's been our experience that if you take a hundred patients, you don't get one single answer from a hundred patients in any disease, no matter how rare it is.

MR. WEINBERG: Hi. Michael Weinberg,

Association for Protection of Cancer Patients. I'm also a science communicator and patient advocate. I'm aware of -- the website clinicaltrials.gov, the trials are registered, and then there's never an update on what goes on and that may contribute to publication bias.

You don't know the results of the clinical trials and what progress is being made on enforcing the rules about making the results available in a timely manner, and also enforce --

DR. MOSCICKI: Do you have an hour or two?

MR. WEINBERG: All right. Well, enforcing the rules, making sanctions for the companies, you know, you can't get another clinical trial until you publish these results or something like that, and in a timely manner. That's the important thing as well.

DR. MOSCICKI: Yeah. So clinicaltrials.gov is not a perfect instrument. I think we would all say that by a long shot. We don't actually run clinicaltrials.gov. I don't know if people know that, but that's run by another federal agency.

And I think while there are rules, those rules are pretty broad and very hard to keep up.

So I think that it behooves us all to think about better ways to do all this.

MS. VON SEGGERN: Yeah, I'm Gayle von Seggern, and I'm a patient advocate for a rare disease that does have a drug now that's effective in treating it, but not approved. So I'm very sympathetic to what you're saying, where you don't want somebody from a company or a sponsor interjecting. But just as an individual, it's very difficult to kind of get our point across of how we feel about this drug and if we're seeking treatment overseas because it's the only way to get it.

You said that the emails -- well, I've definitely done the emails. So I know that's probably a frustrating thing from your point, but as an individual who has no tie to the company that's manufacturing it, it's hard to navigate.

How do we approach you guys without crossing any boundaries?

DR. MOSCICKI: Well, I think if you're one

person all alone, then, yes, you'd have no choice maybe but to do an email or to do a letter. But the greatest power we probably all recognize and the reason that you're here is to band together and to provide a group of people who can provide that opinion and input.

We'll often -- if you talk to our PASE group, they will set something up for you to be able to talk to the right people and express your desires and thoughts and opinions, and for us to listen to them.

MS. VON SEGGERN: Thank you. I am actually part of a little bit of a bigger group than just my little self, but not a really big group. Thank you.

DR. MOSCICKI: I think, yeah, I'm starting to run out of time, but one more. Sure.

FEMALE AUDIENCE MEMBER: I'm part of a rare disease as well, and we don't have anything in the pipeline. But as I'm learning more about this and going to more conferences, I'm amazed at the amount of people who are in a third party industry. And

naively, I'm kind of wondering why pharma has to pay third parties to buffer with the patient community, and I'm wondering if there's a real reason for that.

As a patient, I think for pharma to spend money on a company to help me tell pharma my story is ludicrous. I can go to pharma and tell my story. But is there a reason that all this money is being spent -- and this is at the risk of offending half the people in this room, and I'm sorry. I'm just new to this.

Is it necessary that industry has to hire third parties to play this role of buffer so that they don't get in trouble with FDA?

DR. MOSCICKI: I don't know of anything that says it's necessary. I think for some companies, they may not feel that they have the expertise or experience, and so, therefore, might turn to third parties.

Are you talking about commercial third parties or are you talking about patient advocacy organizations?

FEMALE AUDIENCE MEMBER: Commercial. Just there seems to be a lot of roles, and I would imagine that they're legitimate. I'm just confused --

DR. MOSCICKI: So this is not an FDA viewpoint at all. This is just an observation of someone who's been around a while. And I think, again, it is that a number of these commercial organizations want to sell themselves to companies and say that, you know, we have a lot of expertise here. We've done this. We've done this at other companies. We can help you interact in a professional and appropriate way, and maybe to also keep you out of trouble in terms of not acting in a naked promotional kind of way with the communities.

So it might provide some protection from a legal basis if they -- because it's one thing to ask the opinions of patients, but it's whole nother thing tell patients how great your drug is, or that it's safe, or it's effective. And in fact, that hasn't really been determined.

All right. Thank you.

(Applause.)

DR. WHYTE: Thank you, Dr. Moscicki.

So let's get our clickers ready, and the next question is, which of the following factors does the FDA not consider during the drug approval process? a) biological markers, b) patient-reported outcomes, c) company stock prices, d) clinical outcomes?

This is meant to be an easy question. Rich says it's a trick question. Hopefully, people are paying attention.

(Audience polled.)

DR. WHYTE: Okay. Good, 98 percent say company stock price. I'm glad you're listening.

At this point, we'll turn to patient-focused drug development. Both Dr. Woodcock and Dr. Moscicki have talked about the importance of patient-focused drug development, and I'm delighted to welcome to the stage, Pujita Vaidya, who is the operations research analyst in the Office of Strategic Programs here at CDER. She's been with the FDA since 2012 and is the operation lead on

CDER's Patient-Focused Drug Development Initiative, an effort to, as you're aware, get a better understanding of patient perspectives on a condition and its treatment.

She also works on the development of CDER's benefit-risk framework and its implementation in the new drug review process. Pujita holds a Masters of Public Health from Hopkins, and a bachelor's degree in biochemistry from Wheaton College.

Pujita did not send me her fun fact, so you'll have to offer a fun fact directly. And with that, I welcome Pujita Vaidya to the stage.

(Applause.)

Presentation – Pujita Vaidya

MS. VAIDYA: Thank you, John.

A fun fact? So my parents are actually from Nepal, so I've actually met a living goddess there. In Nepal, they have living goddesses. So I have personally met a living goddess, so I guess that's a fun fact about me.

Well, I'd like to thank you all for inviting

me today, and I'm happy to talk about FDA's Patient-Focused Drug Development Initiative, which is really helping to facilitate FDA dialogue with patients about what really matters most to them.

I would like to apologize in advance; I'm actually not feeling well. So if I start coughing a lot, I'm super sorry.

So as we know, people living with a disease have a direct stake in the outcomes of drug development. They also have a unique ability to contribute input that can inform drug development and evaluation.

So FDA's mechanism to directly obtain patient input have often been limited to discussions related to specific drug applications, as Dr. Moscicki has mentioned, which is through our advisory committee meetings. But there is great value in opening a broader dialogue with patients and their caretakers outside the context of any particular drug or application.

So FDA recognizes a need for more systematic ways of gathering patient perspectives on their

condition and treatment options. This input helps inform the collective understanding of this therapeutic context, as we call it, of drug development, which is important to our role as regulators and the role of developers and others throughout the drug development process.

So today, I'm going to talk to you about the Patient-Focused Drug Development Initiative, which is part of FDA's commitment under the fifth authorization of the Prescription Drug User Fee Act, and as part of our commitment, the Center for Drugs and the Center for Biologics are together convening 24 meetings in a five-year period, and each meeting focuses on specific disease areas.

These meetings are providing us with valuable information, and they also help advance a more systematic approach to gather this type of important patient input more broadly.

Here, you'll see a list of all of the meetings that we've either conducted or are yet to be conducted through fiscal years 2013 and 2017. I do want to give a shout out to our next meeting,

which is on June 10th. It's on neuropathic pain associated with peripheral neuropathy. So if we have advocacy groups and stakeholders here from there, I definitely want to encourage you to come and attend.

When we were trying to determine the set of these disease areas for fiscal years 2013 through 2017, FDA nominated candidates through the Federal Register notice and sought public input on this. Of the meetings conducted to date, we estimate for each meeting, approximately, we have about 30 to 80 patients or patient representatives that have participated in person and about a 100 to 300 people on the webcast.

The PFDD public meetings follow a similar design and format that is tailored for each meeting to account for any unique aspects of drug development for the particular disease area. So thinking about the current state of drug development, specific interests of the FDA review divisions, and the actual needs of the patient population.

They're focused on engaging in a facilitated dialogue to elicit the experiences and perspectives of patients and caretakers. So it's a little different from your typical formal setting here at the FDA when you come in for a meeting. We call it more of a town hall style, where the facilitator actually goes into the audience and tries to make it a more comfortable informal setting where patients are able to open up and talk about their conditions.

We try to gather input in many ways, as I mentioned. So we have the patient panel comments. We have the interactive facilitated discussion. We have webcast and phone lines that we have available, as well, for folks to call in if they're not able to attend in person. And we also have a federal docket that's open up to 60 days after the meeting to kind of allow for anyone who's interested to submit more detailed comments electronically to us.

So the PFDD meetings, we dedicate about three or three-plus hours to the discussion with

patients. Here's just a sample of the type of questions we ask. We ask them to talk about the symptoms that have the most significant impact on daily life.

We ask them to talk about their ability to do specific activities or if specific activities are limited. How well do their current treatment regimens treat the most significant symptoms of their disease? What specific things would they look for in an ideal treatment for your condition?

Going a little broader, thinking about what factors do you take into account when making decisions about using a particular treatment and sometimes even going into discussions about deciding whether they would participate in a clinical trial or not.

So I'd like to highlight the importance of the role of the patient stakeholders in engaging with patients during the planning for the PFDD meetings. We have seen in several cases that advocacy groups have taken the initiative to come together and really coordinate efforts during the

planning.

For example, one example is the narcolepsy groups for our narcolepsy meeting. They actually came together, different advocacy groups came together and formed a separate coalition specifically just for the PFDD meeting called Unite in Narcolepsy.

So such efforts help, coordinated efforts, help in outreach, help in facilitating registration and docket submissions. Also, some organizations have organized transportation because we understand that FDA is not really Metro accessible. It's hard to get to.

So just even if it's from the hotel that patients are staying at to the FDA campus or in some cases there have been -- and for one meeting, folks, they were able to get buses to get patients from Philadelphia and New York to the FDA campus for the particular meeting.

They've also held pre-meeting get-togethers and even conducted pre-meeting webinars to kind of help prepare participants on how to effectively

engage with the FDA.

So we have all these meetings, about half-day, day-long meetings, and the main meeting output, we would say that results from these meetings, is a report called The Voice of the Patient Report. That captures the patient input in the meeting in the participants' own words. So really, in the actual patients' own voice.

This input, by providing important patient context, can support FDA staff as they conduct benefit-risk assessments for products under review, advise drug sponsors on their drug development programs, or identify opportunities for further discussion.

We also believe these meetings can have value to drug development more broadly. For example, by helping to identify areas of unmet need such as aspects of patients' conditions that is not currently being addressed in current therapies. This input may also help developers as they identify or create tools used to measure the benefit of potential therapies. And we have seen

the potential in the meetings to help raise awareness within the patient community.

So FDA's really grateful to patients, caregivers, and others who so thoughtfully and courageously share their experiences and perspectives to these patient-focused drug development meetings. And we are encouraged by the positive feedback that we have received, demonstrating that many patients and others take away from these meetings a feeling of being listened to and being valued.

So that being said, we recognize that 24 disease area FDA-led meetings doesn't really cover the breadth of diseases that are out there, and there has been a growing external interest in expanding the efforts to gather patient input in support of drug development and evaluation.

So to help expand the benefits of the Patient-Focused Drug Development Initiative, we welcome patient organizations to identify and organize patient-focused collaborations to generate public input on other disease areas outside of the

24 disease areas that FDA has identified.

We, as in FDA, are open to participating in a well-designed and well-conducted meeting that is planned by using the process established by the FDA's patient-focused drug development as a model for those. And since this will be your meeting, the meeting and any resulting products, like any kind of summary reports that you put out, will not be considered FDA sponsored or FDA endorsed.

So given the expanse of the diseases affecting the U.S. patient population and the effort required to conduct a successful patient-focused drug development meeting, externally patient-focused meetings should target disease areas where there's an identified need for patient input on topics related to drug development.

So when identifying a disease area, we ask that you think about, is the disease chronic, symptomatic, or affects functioning and activities of daily living. Think about disease areas for which aspects of the disease are not formally

captured in clinical trials, and disease areas for which there are currently no therapies or very few therapies out there.

Also, the target patient population should be considered and clearly defined, so identifying any needs to focus on particular sub-populations such as children or the pediatric folks, or people with metastatic forms of a particular disease.

Eventually, the success of an externally-led, patient-focused meeting will require a joint and aligned effort by all interested stakeholders. If there are several active groups out there for a particular condition, we ask that you come together and propose one meeting, rather than us getting several requests for the same meeting to be organized.

There are some other considerations when thinking about conducting your own externally-led, patient-focused drug development meeting. Once you are ready to reach out to the FDA, we ask that you submit a letter of intent communicating the importance of the meeting and your proposed plans

for the meeting.

We ask that you submit the letter of intent approximately one year before the anticipated meeting date to give enough time for the FDA to review your proposal, provide any type of feedback, and work with you to put together a well-organized meeting.

Along those lines, when deciding FDA's level of participation, we will also take into consideration the following, so thinking about specific need for more input from the patient perspectives, recent interactions with patient stakeholders, the meeting time and location, and the actual FDA staff capacity.

Finally, here is some additional information that we have. All of the information that I just presented is actually on our website. We have our externally-led, patient-focused drug development meetings website where you'll find the guidelines to submitting a letter of intent.

Any other questions you may have should be answered on that page, and if they're not, please

do feel free to email us. If you want to look back and go see what we've done with the FDA-led meetings, please visit FDA's PFDD meetings website that we.

All previously conducted meeting materials there such as agendas, discussion questions, the actual webcasts; the Voice of the Patient Report that we put out, that's also on our website. So please go and take a look at that.

Like I said, if you have any questions, email us. Our email is patientfocus@fda.hhs.gov, and those emails will come to our office, which is CDER's Office of Strategic Programs, and we're the ones leading the patient-focused, drug development effort. And if we don't have the answer to your question, we'll be able to connect you to the right folks here at the FDA.

That being said, I do want to acknowledge our team. Like I said, Office of Strategic Programs, we're the ones that lead this initiative. Theresa Mullin, who's the director of this office, is the CDER lead for this initiative. And all of

our team members have been very important in making this initiative a success.

Along with that, we work very closely with our Office of New Drugs colleagues, our Professional Affairs and Stakeholder Engagement staff, and other offices throughout the agency, such as Office of Health and Constituent Affairs, Office of Rare Diseases, et cetera. So thank you so much.

(Applause.)

DR. WHYTE: Thank you. We have a few minutes -- do you have a few minutes for questions, Pujita? There is a question from the Web, so we'll start with that with Dr. Damon Green. And then if you have questions, please feel free to come to the mics or raise your hand, and we'll come to you.

DR. GREEN: So there is one question that you probably answered in your presentation, but for the sake of clarity, she asked, "How does FDA choose the disease for focus at the public workshops for patient-focused drug development?"

MS. VAIDYA: So for the meetings through

fiscal years 2013 through 2015, we initially put out a Federal Register notice back in April 2012 -- I think; it was a while back -- where we nominated disease areas and solicited input from the public, basically.

We then analyzed the comments that we got, went back to the review divisions, and then identified -- for the first three years of PDUFA, we identified 16 disease areas to be the disease area meetings for that time frame. Then we had a very similar process in 2015 to identify the disease areas for 2016 through 2017.

So it's a public process that we use, and then for the second process, we identified eight more disease areas. So now we have a total of 24 meetings that we're doing, which is four more than we did actually commit to.

MS. BARNES: And just to add to that, Pujita, you guys also took public input on that list. So a lot of patient advocacy groups actually suggested that the certain diseases be added. So we did that in the pulmonary fibrosis area, and

there were others that did it. So thankfully, FDA did take suggestions.

MS. VAIDYA: Yes. Thank you.

Next question?

MR. BUTLER: Actually Craig Butler, Cooley's Anemia Foundation. Two related questions, and I apologize if you answered these, and I just missed them.

You've got your internally-led meetings scheduled through 2017. Are there plans to have another round of those beyond 2017 or is that it? And then, referring to the externally-led meetings, is there a level of importance in terms of whether the FDA is able to attend these meetings as to location?

Do we need to try to schedule them here in the D.C. area or if one was scheduled elsewhere, other places in the country, would the FDA still consider sending a representative to them?

MS. VAIDYA: So to answer your first question, we have not yet established a plan for any other meetings beyond fiscal year '17, so it's

still in the works right now and we're still in the planning phases for that.

Then to answer your second question, we do ask that when you do think about planning these externally-led meetings, that if they remain in the -- so D.C., Maryland, Virginia area, it is more accessible to our FDA reviewers, and it is easier for them to attend; whereas if it's somewhere, elsewhere, in the country, it may be a little more difficult, and we may have a harder time getting at least the FDA representation that you would want there. So yes.

MR. BUTLER: Thank you.

MS. VAIDYA: You're welcome.

DR. WHYTE: All right.

MS. VAIDYA: Thank you so much.

DR. WHYTE: Thank you, Pujita.

(Applause.)

DR. WHYTE: Okay. We're going to take a break until 10:40. Again, a reminder to pre-order lunch if you want to be able to have lunch. There is a color-coded card at each of the tables. So

after lunch, at 1:00, we are going to play Jeopardy, and you're probably wondering how are we going to play Jeopardy with all these people.

There are four microphones up here. We're going to have four teams, and the four teams are the four different colors. It's great to meet FDA folks, but it's also great for many of you to meet each other. So ultimately, we're going to have to have a representative from each of the colored teams.

You'll have time over lunch to work that out, but the afternoon is going to be fun. I know that's hard to believe that it's going to be fun at an FDA meeting. And we did have a test rehearsal yesterday; I mean, I hope it worked out.

(Laughter.)

DR. WHYTE: But the plan is to do Jeopardy at 1:00. So take some time, get some coffee now, order lunch if you haven't, and I'll see you all promptly in 20 minutes at 10:40. Thank you.

(Whereupon, at 10:18 a.m., a recess was taken).

DR. WHYTE: Okay, if everyone can come back and return to their seats, we're going to go ahead and get started.

We're going to start with a clicker question, so please come back to your seats and get ready for another quiz. And we'll start off with, During a drug shortage the FDA can: a) manufacture more drugs to meet demand, b) import drugs from Europe, c) force manufacturers to produce more drugs, or d) none of the above.

I see some people clicking multiple times. It doesn't work. Only one vote per person. This is not Texas.

(Laughter.)

(Audience polled.)

DR. WHYTE: All right. Let's see what our numbers are. Okay, none of the above. That answer is incorrect.

Who are my people that voted B? Okay. You're the smarty pants. The answer is B -- at least I hope it is; Val will correct me if I'm wrong -- to import drugs from Europe.

So now we're going to hear from Captain Valerie Jensen, the associate director of the drug shortages staff. She received a B.S. degree in pharmacy from the University of Iowa in 1990. She completed a residency in ambulatory care at the White River Indian Health Service Hospital in White River, Arizona.

She's worked as a clinical pharmacist for the Indian Health Services Hospital in Arizona and New Mexico for nine years before joining the FDA, and she's been with the drug shortages staff for over 16 years.

Her fun fact, she was telling me prior to coming in, she's like, "I'm a running maniac." And I'm like, "Well, what's a maniac?"

This is how I know she's a running maniac, because she's like, "I've only done five marathons." Well, only five marathons? I wish I'd done one.

But with that, I will gladly welcome Captain Valerie Jensen to the stage. Thank you.

(Applause.)

Presentation – Valerie Jensen

CAPT JENSEN: All right. Thanks, John.

Good morning everyone. And that was a good answer, to say none of the above, because people aren't really aware sometimes of our ability to do the imports, and I'll talk about that a little bit more as we go along.

First of all, I'm Val Jensen. I'm the associate director for Drug Shortages, and I'll talk to you today about our shortage role, what FDA does about shortages, as well as what the manufacturers' responsibilities are, and also how to report a shortage for patients and for people out there that have experienced this.

Our mission in FDA, we definitely want to prevent shortages if at all possible. We also do a lot of outreach. We do a lot of stakeholder outreach because we know how much impact this has on all of you and on the patients that you serve.

Our role, really, FDA takes this really seriously. We know how bad it's been. We know how bad shortages have been. We've actually expanded

our program. We have 13 full-time people now that work solely on drug shortage.

Within FDA, there are many, many people that work on shortages. We've got a large group. You can see here the list of different groups, and you're probably learning about some of these groups from the talks that you've had here. There's about 25 people at any given time that are working on shortages, and that's including our immediate response team, as well as the chemists, the microbiologists, all the different groups that come into a shortage.

One thing I should mention that has really been the biggest help that we've had with shortages has been a new law that went into effect in 2012. We talked to the Congress a lot about how bad the problem was and what might help it. And what we kept telling everyone that would listen to us is that we weren't hearing about shortages before 2012. We weren't hearing about them until they were already in effect.

That's way too late. So once the pharmacist

is noticing the shelf is bare, once the patient isn't able to fill their prescription, that's way too late. We needed to have early notification. We needed companies to tell us when they were having some type of problem, which was not any type of law. There was no law about that. Companies were basically having a problem, running out, and then we would find out about the shortage after it was already a shortage.

This new law was enacted in 2012 called -- it's a long name -- Food and Drug Administration Safety and Innovation Act, FDASIA, and that's really helped us. So now companies are required to tell us when they know they're going to have any type of supply disruption. That way, we can use our tools, use everything that we can do, to work with the companies to hopefully prevent the shortage. We also have a strategic plan that we developed ourselves that talks about our goals and the goals for industry.

All of our information about shortages, if you want to know what's in shortage, is on our

website. That's the address right there. We also have a mobile application that was recently developed, so that will actually give you real-time information. You can get feeds into that on what's in shortage right now.

One thing I'll just put out right in front is if you're experiencing a shortage or you know about something that a patient isn't able to get, let us know. Hopefully, it's on our website. If you don't see it on our website, definitely let us know. That really helps us. Unfortunately, sometimes companies aren't as communicative as they should be, so we definitely want to know from patients and patient advocates if you see something.

Our information; how do we get information and how do we even know if there is a shortage? We're not only hearing from the companies on when there's a potential supply disruption, we also have information that we get from other sources. We can get information from -- and this is really basically a picture of the supply chain. We can

get information from the wholesalers. We can find out how much is normally needed to fulfill the market, so we get that from a tool called IMS.

When we determine that there's a shortage, what we're looking at is all the information that comes in to us, all the manufacturer information, and then we're looking at how much is being produced, how much inventory, how much is out there, compared with the national demand. And we get that national demand data that we purchased from IMS Health.

If there's a gap and we're hearing from patients, we're hearing that there's a disruption, it's a shortage, and then we'll post it on our website.

Some of the other parts of the supply chain that are really not as -- well, we just don't get as much information; repackagers. You hear about the gray market, some of the secondary supply chain. We don't have a lot of information about what goes into that. We try to get information. Really, our primary source of information is the

actual manufacturers.

How bad has the shortage problem been and how bad is it now? Our spike in shortages happened in 2011, where we had 251 shortages that were reported and confirmed. That number was horrible. That was mainly due to large manufacturers.

We had several large manufacturers that were generic. They were mostly making sterile injectables, hospital drugs, had major quality problems, decided to shut down to fix those problems, and it really just cascaded into this terrible shortage that occurred.

Two hundred and fifty one drugs were in shortage that year. We'll still recovering from that, really. Most of those are resolved now, but some are still kind of shaky because it's taken a while to gather manufacturers to come in and make those drugs.

So the numbers are going down. This past year, only 26; that sounds like a good number. It's still high because some of those drugs were really important. We don't consider the problem

over. And this is just a graphic just to show you things look really good.

Another thing I should mention -- and I'll talk about this a little bit later, too -- but the reason for lower numbers is not only because things are getting a little bit better. We're seeing fewer numbers of new shortages. But the big reason is that we're able to prevent more shortages.

We're still getting really large numbers of notices from manufacturers, and then being able to work with those manufacturers and other manufacturers to fill the gap early on before the shortage happens, that's been successful.

This just shows you the reasons, and really it's been mostly quality problems. That's been our main reason for shortages. When you talk about quality, people ask what that is. And most of these are not just minor issues. Most of them are fairly serious, things like sterility where the product -- obviously an injectable drug that's going to be injected into a patient has to be sterile. Anything can really happen along the way

during the manufacturing, but sterility is a big issue.

Particulates, so things break off in the manufacturing process or get in there that shouldn't be in there, like glass or metal. Those have been serious issues as well.

Our focus is patients. We want to make sure that not only are we continuing supply, but we want to make sure that it's a safe supply, that patients aren't put at risk.

This is our drug shortage definition, and I mentioned that. It's really that supply is just not meeting demand.

Our medical necessity definition is important, really, because that helps us prioritize. So we're looking at mostly drugs that treat serious disease. It's not that we don't care about anything else. There are some drugs that maybe don't meet this definition, but they're still important to patients. So we're still working on those. It's just that we have to prioritize.

Some things obviously take longer to resolve

than others. We always consider risk to patients. So if there's a sterility issue that's really hard to resolve, the company's got to do several different processes to ensure that that manufacturing line is safer for producing drugs, so that can take some time.

Some other kind of quicker fixes we've been able to work through. One example would be with the particulate issue. A company, if they report particulates -- so they have to figure out what's in there and what impact does that have. And even if it's a sterile drug, what they can do and they have done, is propose a filter.

So they can either introduce a filter during the manufacturing process or they can also introduce a filter at the bedside of the patient if it's a hospital drug; so ship the filter with the drug, and prove to FDA, based on data, that that filter will remove the particulate.

That's something that we've done fairly commonly in recent years, especially with older facilities where things are kind of going bad with

the lines and they need to upgrade their lines, but in the meantime, we want to keep the drugs available. So that's something that has worked.

This is just talking about the quality issues, the GMPs. You've probably heard of that, the good manufacturing practices that companies have to maintain. Those can be the high-risk issues. They're things that we're going to work through with the company.

There's also kind of lower-risk issues that happen. Sometimes the wrong label gets put on the drug, or the wrong NDC number, or the wrong expiration date. Those are pretty easy to deal with. We work with those with companies all the time. So basically, if that happens, we can let them put a sticker over it, send a letter just saying why that occurred or that that did occur.

What we can require? We can require notification for sure. And if a company doesn't notify us, so they don't let us know at all that they had this supply breakdown, we don't have a fine or anything like that. But what we do is we

do a public wall of shame. So we actually send them a letter. We tell them you failed to notify us, and why that was so important that they notify us. This caused a horrible shortage for patients. This was a big impact on hospitals, and on pharmacies, and on patients.

We put that letter on our website. Companies don't want to get that letter. They don't want the public to see that letter. It looks bad for them. We've had to send two of those. We hope we don't have to send any more of those.

Another thing we can require is any changes that the company has to make. So if they want to make a change to their manufacturing line, or they want to add a new supplier, or add a new manufacturing site, those things have to be reported to us. That's good, because if it's a shortage issue, we'll expedite review of that.

We can't require a company to make more drug. We can't require them to make more of a drug, or how much, or where it goes to. We wish we could require those things.

When we first hear about the shortage, of course we make sure it is a shortage. We contact all the companies that make that drug. We figure out what the supply situation is. We prioritize based on medical necessity.

If a whole line is going down at a firm, a whole manufacturing line, and that manufacturing line may make 20, 30 drugs, we're going to make sure we focus on the ones that are absolutely needed. What are the greatest market shares? What are the greatest public health need? And then we're going to work across the agency on a remediation, on a fix, and with the company.

Of course, the thing is we would never want to have a company sending out a drug, even if there are risks involved. We want to make sure that those risks are mitigated, so there's not any patient harm.

This is just all the groups that we work with. Mainly, the bottom row, we're working mostly with manufacturers. We're also reaching out. We want to make sure we get information out on our

website and to groups that need to know.

This I've talked about, the averted or prevented shortages, which is really our primary goal. Of course, we want to do everything possible early on to try to minimize effect and minimize impact.

We've been successful at that. Our prevented numbers went way up in 2012 right after the notification requirement came out. They've gone kind of down. We just need to keep getting the word out to companies. Let us know early, because the earlier the better. We don't even care if they over-report. If they tell us early on that, hey, we may have this issue six months down the road, FDA what do you think, we're glad to hear those messages.

We can't always prevent. Obviously, sometimes something will happen that's really catastrophic, something like a sterility problem or a whole plant has a problem, or a line, a production line. Sometimes those are really hard to fix. But again, we'll continue to work with the

company until it's resolved.

So what are the things that we can do with the company, once they report the shortage? Regulatory discretion is one tool. What that means is -- like the example with the filter, if there's something wrong with the product, a defect with the product, wrong label, has a particulate, something went wrong with the stability and it needs a shorter expiration date, or something like, then we'll work with the company, make sure we can minimize risk.

If there's, really, no significant risk for patients, then what we can do is have the company go ahead and release the lot while they're fixing the problem, because they have to fix the problem for future; but in the meantime, get the drug out for patients, and also inform, because we want healthcare professionals and patients to know what the risk is.

So we'll have a letter sent out with the product that says what was wrong with it, and that'll go on our website as well. That's

something we've had to do quite a bit.

The other thing we can do is have companies do extra testing if there's a potential risk. They can also have a third party come in, like a consultant to help with fixing a problem.

The second tool we have is if we hear from one firm that they're out of product, we can go out to the other manufacturers that make that product and ask them to increase production. It's something that we have to be careful because we can't tell the other firms what happened at the first firm, and we can't name the first firm.

So we just have to say, we know there's going to be a supply gap. We know it's going to be about this much, and this is the duration; can you meet this need? And that's worked as well.

We can expedite review, as I mentioned. So anything that the companies need to increase production, we'll expedite.

The other thing -- so this was the answer to that question that John asked -- as far as import, it's something we've done 22 times over the past

few years. When we don't have a manufacturer that can make the drug in the U.S. and we have to look for a source, because it's a medically necessary drug, it's needed for patients, we'll look for sources overseas that we feel comfortable with.

So we'll go out and we'll inspect those sites, or we have foreign regulatory inspection that we can rely on. And we'll evaluate that product really carefully so that we know any differences with that product between that product and the approved product. Then, if we can find a firm that meets all of FDA's standards and we feel comfortable with that product, then we would temporarily allow the import of that product.

So that company would bring it in. FDA's not importing it; it would be the company importing it, and we make that information known on our website. Again, patients and healthcare professionals need to know they're taking a drug that's not FDA approved.

We would have a letter sent with that product, and that's placed on our website as well.

That's something that's really worked. In situations where we really have no other choice, it's worked.

The role of industry, again, we need them to let us know when there's any potential issue. We need them to update our website, which they've been a lot better at doing, and then working with us. Especially, in 2011-2012, when we had those shutdowns of large manufacturers, that's something we really want to avoid.

So it's something that we're working with our chemists here and our manufacturing experts here to work really closely with the companies when they're having those issues because if we can keep them going, keep certain lines going, that are still meeting all of our standards while they fix their problems, that's really the goal.

So our role again, we need to perform risk-based analysis. We need to make sure that we find innovative ways and ways to address the shortages with the manufacturers and prevent, and then we need to get the message out to patients and

to healthcare professionals about the shortage.

What do we think will happen over the next few years? We keep getting asked if the shortage problem is going to continue to subside, are we going to have this over at some point to a level of zero, which we would love to have.

We don't see that happening. We know that even this year we've continued to have some very serious shortages. Last year, we had a shortage of IV saline, which people might have heard of. Those are those large bags of IV salt water that every single patient gets when they go in the hospital.

We had a shortage of that, which is really unreal, because we kept getting asked, how can there be a shortage of salt water? But again, it's that really complicated process of making a sterile drug. So those bags from start to finish have to be filled with the sterile saline. They have to continue through that process, and they get placed on sterility. It takes about three weeks to make one batch.

Demand had increased at a time when the

companies were at capacity, so they really couldn't keep up with demand, and things just snowballed, and we went into that terrible shortage. So in that case, that was one of the worst shortages we've had, and we had to import from three different firms overseas and Europe.

So again, we don't see this as over. We think these things can continue to happen. We just want to make sure that we're set up in FDA to be able to address them. And we feel like we do have the resources to do that, and we just want to continue to make sure that you all are informed, too, when things are happening.

Again, the manufacturers' role, we do work with manufacturer groups. We work with their trade groups as well as individual manufacturers. We're trying to work with them on best practices and how some firms have avoided shortages and sharing those practices with other firms, and just making sure firms are aware that they can contact FDA and that we will help them.

These are all the contact information

websites that you might be interested in. This is our CDER drug shortage email address. We have a phone number as well. Then CBER, the Center for Biologics, that would be for vaccines, blood products, and then some other contact information.

Here's some more information that's on our website if you're interested in other links. But I'll be glad to turn this over for questions. So any questions that you have, I'll take. Thank you.

(Applause.)

CAPT JENSEN: Do you have any questions? Okay, thank you.

DR. WHYTE: We can send you them if they come up. Thank you, Val.

CAPT JENSEN: That's fine.

DR. WHYTE: We're going to have a slight deviation in the script. Captain Jason Woo is going to talk about generic drugs shortly. But beforehand, recognizing, today's all about the Center for Drugs. But as I showed you in that first slide that nobody could see of the vastness of the FDA, we're also involved with devices. We

also regulate devices. We have a role in the regulation of tobacco, biologics.

There's lots of ways that patient input can be incorporated into decision-making, and there are various touch points, as confusing as it can be at times, for patients to engage.

My colleague in the Office of Health and Constituent Affairs is Heidi Marchand, and she's going to talk just very briefly, just a few minutes, about other ways that folks can interact with the agency even when it's on issues of drugs, but when it's also other areas as well.

Heidi has over 13 years of experience at the FDA. She began as a review officer in the Division of Drug Marketing and Communications, and now she's an assistant commissioner and is responsible for several programs, including, as many of you are familiar with, the Patients Representative Program, Patient and Stakeholder Liaison Program, and the MedWatch program that Hank Hoang mentioned.

She also oversees interactions with various multiple stakeholders, including consumers and

healthcare professionals in the industry. And prior to the FDA, Heidi has worked in the biopharmaceutical industry holding leadership positions at Novartis, Pfizer, Amgen, where she's worked with the U.S., Europe, on Japanese authority. So she knows very well where drugs are approved first.

Now, her fun fact -- and you would not have expected to hear this -- is Heidi is a Led Zeppelin fan. And I was confusing that with the Grateful Dead yesterday and asking her if she was traipsing around the country going to Led Zeppelin bands. She's like, "John, that's the Grateful Dead."

She's a Led Zeppelin fan, and she is also very involved in yoga, so Namaste. Heidi Marchand.

(Applause.)

Presentation – Heidi Marchand

DR. MARCHAND: Well, John, thank you very much, and thank you very much for inviting me to say a few words. And I certainly want to welcome all of the groups that are here today, interested in understanding how to engage with FDA and the

best practices for doing so.

It's been just really great to see the organization under CDER grow under your leadership, and to see this room filled with folks that are interested. I know you also have a number of individuals that are signed up on the webcast and are listening to the conversation taking place. So kudos, and I think it'll help to clarify and to get more and more folks engaged.

Just very high level, our office has a long history of being involved with the Patient Representative Program. I believe there might be a few patient representatives who are in the audience today or listening.

There are about 200 different special government employees that are involved with that program, and we do participate, or as a special government employee those patient representatives participate on the committee as a member. It's one individual patient. Some instances, it's been two.

But certainly, we recognize that in some cases, that's not the complete voice of all

patients around the table that are interested in seeing the development. So building, and coming forward, and having more interactions, and hearing more with the patient-focused, drug development meetings that have been taking place, has been a fantastic way to increase the amount of involvement and to hear more and more voices around the table.

It certainly is an important program that we've had, and we do encourage not only patient representatives to come forth and participate in that regard, but also there's an opportunity for public comment at those meetings. And we do encourage, and hopefully these kinds of programs help to better understand points of interest that the agency would like to hear from you.

I'll just also mention, we also manage the Patient Network web pages. We've got a newsletter you can sign up for on our Patient Network webpage that we've got. We have a very nice way for you to enter into a docket, if you're interested in making comments on many of the different proposals that FDA puts forward seeking public comment.

Again, the Center for Drugs, the Center for Devices, Center for Biologics, and in some instances patient and advocates are very interested in comments with regards to foods and other guidances and regs that affect those areas as well.

So I hope you enjoy the day. I know it's a dynamic program and looking forward to hearing very positive outcome and results from it. So thanks very much, John.

(Applause.)

DR. WHYTE: Thank you, Heidi.

The question has come up whether we will make the slides available, because I do know a lot of folks were taking pictures, especially early on during the NDA process, and we do plan to make the slides available on our home page. And remember, the handouts that we gave out has a lot of good information as well.

So get your clickers ready. It's our last clicker question before lunch. It's a true/false question, and it's, generic drugs are as safe and effective as their brand counterparts?

True or false, generic drugs are as safe and effective as their brand counterparts. True or false?

While you're thinking and answering, I want to thank Captain Jason Woo for his indulgence in letting us revise the agenda a little. So who says the FDA's inflexible when we folks willing to change their schedule?

(Audience polled.)

DR. WHYTE: Okay. Where are you 8 percent? Okay, you're going to learn a little in this lecture. I didn't say it was anonymous. Okay. But it is.

Captain Jason Woo is going to talk about busting the myths of generic drugs, and this is a common myth. Dr. Woo's experience with the FDA includes positions in the Division of Dietary Supplement and Programs, and in Scientific and Medical Affairs, and the Office of Compliance.

From 2012 to 2013, he oversaw contraceptive product development and the Contraceptive Clinical Trials Network at NIH. He returned to FDA and CDER

in the Office of Generic Drugs to help implement the Generic Drug User Fee Amendment known as GDUFA of 2012.

Captain Woo maintains his clinical practice at the Washington Hospital Center, as well as at Bread for the City free clinic in Washington, D.C. Please join me in welcoming Captain Jason Woo.

(Applause.)

Presentation – Jason Woo

CAPT WOO: Just so you know, my fun fact is I know how to tie a bowtie. Right, John? It's an inside joke; just had to teach him.

Busting the myths. What are these myths and why are they there. To be honest, I really want to thank John for this opportunity to hear from you all. I think this is going to be a great learning opportunity for me because I have a bias. My disclaimer is I use generics, and I use them a lot.

I started my clinical career with Union Health Service in the rural southwest part of the United States. I've been on multiple deployments, two emergency response missions like Katrina or

Hurricane Ike, and also a number of underserved areas in West Virginia, along the Rio Grande border with Texas and Mexico.

Lastly, as John mentioned, I maintain my clinical practice at a free clinic, or what has been a historically free clinic, in the District since the Affordable Care Act. In all those environments, without generic drugs, I would not be able to effectively practice. I mean, I could not prescribe medications that my patients would fill.

In fact, the last time I was down at the Rio Grande, where we set up the clinic was in a school, and right down the street was one of those Big Box stores that has the $4 and $10 generic programs. And the pharmacist came over after his shift to meet me, because he was like, Who's this Dr. Woo prescribing all these drugs, generic drug products?

I'm just always amazed by how many prescription on these missions, I see either the prescription itself or an empty container where patients just haven't gone back to get it filled because they can't afford it.

So as a patient and a provider, I absolutely think that generics are safe, effective, and sometimes better for my patients, just because they're going to get them filled.

So I know I have that bias, and I'm really looking forward to hearing from you all what the concerns are about what myths there are or why that we still have those myths.

To begin, let me just share some information about the generic industry. This is one of those facts that the generic industry likes to promote, that generics generally cost about 80 percent less than their brand counterparts. And one of the things that they like to add to that is that over the last 10 years, generics have probably saved the American consumer about $1.5 trillion dollars. I mean, $1.5 trillion; that's a lot.

That works out to about $3 billion a week. And as the late congressman and senator from Illinois, Everett Dirksen once said, "A billion here, a billion there, pretty soon you're talking some real money."

So that's a good chunk of change, and how do we get there? Well, it starts by the fact that 8 out of every 10 prescriptions in the U.S. is filled by a generic medication. And that only happens if patients and providers are confident that the drug that they're getting is the same quality and performs the same in the body and with respect to treating the condition as the brand counterpart.

Where does that confidence come from? Well, we're the FDA, right? We like to think it comes from our approval process and our regulatory oversight. To be approved, a generic drug has to be the same ingredient, the same strength, the same dosage form, and administered in the same route as the brand counterpart.

After a company can show that, it also has to prove to us that it's therapeutically equivalent. And when I say therapeutically equivalent, that means we expect it to work the same on the disease condition and to perform the same in the patient as the brand counterpart.

Most of the time, to prove that, we're requiring the applicant to demonstrate that they are bioequivalent, and we'll get into all the science and details. But that's how we infer therapeutic equivalence. After they've met that bar, they also have to demonstrate that they're meeting the same quality manufacturing, testing, labeling, packaging standards that are required for the brand counterpart.

So that's where we hope the confidence comes from, that our strict, tight standards for approval, are what provide some of that confidence.

But we also know that's not the end of the story. When we approve a drug, a generic drug in particular, we're doing it with the best science that we have available at the time. We know that our understanding of the disease condition or how a drug works in body probably evolves over time, certainly as the drug is used in a wider and broader population.

So we absolutely know we need to hear from you to understand what are the concerns that are

rising up, so reporting via adverse events, either side effects or that the product's not working, or other problems that you're running into. We need to hear about those, and we want to hear about those because that's the only way we can continuously actively survey the landscape and monitor it for potential problems that may be developing as a drug is used more broadly and in a wider population.

So please, this is one of the things, we're begging to hear from you. Use the MedWatch system, the other types of accessing FDA, or letting us know about problems that you're concerned about.

One of the cool things about our generic drug program is we're the only user fee program that actually has a funded regulatory research program. So as part of that program, every year we hold a public meeting. This year it's on May 20th; I apologize for the small print on that.

But we need to hear from you all about what are the concerns that you have regarding generic drugs and how they get approved. I think the first

year we had the program, back in 2013, I think we had 13 areas of priorities, and we realized that was probably a little bit complicated.

So what we've done is we boiled that down to five general areas of priorities, and this falls into postmarket surveillance and evaluation of generic drugs; demonstrating therapeutic equivalence of complex or locally acting drugs; the standards that we use for determining therapeutic equivalence, as well as the computational and analytical tools that are available to support all these research areas.

Even if you don't have a question or concern, it's worth listening in to the webinar that's held on May 20th with this public meeting, because there's really some very interesting questions that are posed to use scientifically.

I think a lot of the attention in CDER ends up focusing on the interesting clinical questions regarding approval of the new drugs. I will tell you, since coming back to the agency, that the science of equivalence is equally invigorating,

particularly when we're dealing with complex dosage forms, patches, inhalers, or locally acting drugs, things that only are supposed to affect the diagnosis or the problem in the GI tract or in the eye.

There's some really interesting science that's going on with this program, so I encourage you, even if you don't have a concern, it's worthwhile listening in to the webinar to hear what's presented in the topics there.

Another thing that's really kind of cool, we have an app -- I forgot the drug shortages also had an app, and I really wanted to show it to you on my iPhone, but even though I've got five bars, my service provider doesn't seem to allow it here.

So the Orange Book Express app came out last October-November. And why this is helpful is it lets you know if there are generic versions of the medication that you may be taking. This is -- when you're opening the app up -- what it looks like, and then you can put in any active ingredient or drug, either by proprietary name or generic name.

This is the type of information that will come up, either on the brand side or the generic side. It will tell you who markets this, what strengths are available, and what dosage forms are. The only difference that you'll notice between the brand and the generic is the application number: N obviously for the brands, and A, the abbreviated new drug for the generic.

Also, what's helpful is understanding if there is no generic. So when there is no generic, what you will see is that there's nothing entered under the TE code, and TE standing for therapeutic equivalence. This is the only product at this dosage strength that is available.

There is one nuance about this, because the drugs are approved based on, as I mentioned, the strength of the dose. So there are products, say, for example, that may have generics approved for 100-milligram dose, but not for the 200-milligram dose.

That's actually something I found quite a lot in my practice, where somebody was prescribed

200 milligrams, and the only thing available was the brand. Well, okay. It was a lot cheaper for them to take two of the 100-milligram tablets. And that's just one of those practice in medicine things that sometimes people don't think about, particularly in some of these populations.

So that's where you go to understand if there is or is not a generic equivalent.

I also circled the patent and exclusivity information that's available here, because if you're wondering why there might not be a generic available, this is the first place you start your investigation into understanding what might limit the availability of a generic form on the market. And I'll come back to that at the end.

The last thing I want to mention is that we are currently in year 4 of 5 implementing the Generic Drug User Fee Amendments of 2012. This has been a period of incredible change for our office and other parts of CDER and FDA as well. Our office was torn in half. We doubled the size of it again. We hired over 300 people. We implemented a

brand new reporting system. We had all kinds of goals to meet.

It's been a challenging time, but I think we're very happy to say we're very pleased with the progress that we've made, certainly in meeting all of our commitments to the amendments and all our goals for it. But more importantly, improving the transparency and clarity of what the standards are for getting generics approved and how and where we are in meeting that.

In addition, I think we've actually improved our responsiveness to everyone about questions around generics. The last piece of information that I'm sharing is the generics drugs at FDA email site. If you have a question about generics, email it there. If we don't know the answer, we'll make sure to get it to the office in or part of CDER, FDA that's responsible for answering that question. So please, we welcome your input.

With that, I want to get back to what are your questions or issues? Because again, I know I have a bias about generics. I absolutely believe

they're effective, they're quality medications. But we need to know, what is it that you're concerned about, so we can do a better job of effectively engaging or addressing those issues. Thank you.

MR. BUTLER: Craig Butler, Cooley's Anemia Foundation. Trying to figure out the shortest way to put this. I tend to agree that the generics are safe and effective, but I know with our patient population, there may be some difference of opinion on what effective means and on, therefore, the FDA's ability to understand that there may be some problems with efficacy.

In particular, some of our patients use a drug called deferoxamine, which in its brand name form, they tend to have no problems with. But many report having problems with it in the generic form. It's a powder that has to be mixed and injected subcutaneously, and many of them report clumps and irritations that they find with the generic version that they don't find with the brand name version. But they don't consider it necessarily an adverse

event, so it's not something that they report.

So I'm just wondering if there is some mechanism that may be needed to clarify what kind of information the FDA needs.

CAPT WOO: Yes. That's a great question because it asks actual patient use, right? The drug is maybe approved based on the standards that we understand of how the drug is typically used and with certain diluents or in certain environments.

We don't necessarily cover all those upfront, so it's important that we understand and we hear from you about those times when it's either -- it's not necessarily an adverse event, but it's a problem with actually using the medication. We absolutely need to hear about those. Right?

Other examples are inhalers that just don't quite function the same way. There's a clicking problem, and sometimes folks don't feel like they're getting the same dose as they might with the brand. It might have been approved based on what we saw, but there might be some aspect about

the actual use of it that is more challenging for patients.

So we absolutely need to hear about that, and those are part of the things that we engage in the research area. So I think your point is well taken. We certainly want to hear about those cases.

Like I said, we monitor those reports regularly. Every two weeks, we're tracking what's changed in the adverse events. We're comparing it to what's been reported when the product may have first came out to what we're seeing now. So getting that type of information is very helpful.

Yes?

DR. GREEN: What is the role of the FDA in assuring equity in the availability of effective drug therapies when drugs are expensive and generics are not available?

CAPT WOO: So repeating the question, it's what's the FDA's responsibility when there is not a generic available and there is an expensive brand out there? Yes. That gets back to my slide about

the patents and exclusivities.

Generics became possible after the 1984 Hatch-Waxman legislation, and the challenge with figuring out who is eligible for approval. In some of the legislation that's been litigated -- sorry, the litigation that's been addressed -- in 2006, one my favorite quotes is by Judge Robert Titus who was presented with information about the Hatch-Waxman Act, and his quote was, "There's a special place in hell for people who write stuff like this."

(Laughter.)

CAPT WOO: The patent exclusivities, it's not just that a patent may expire. It may be that there is some agreement between a firm and a generic manufacturer that may allow a generic to be approved before those expire.

That is all in the realm of the legal area. I don't want to necessarily give a bad impression, but Shakespeare said, "First kill all lawyers." We have good lawyers, too, that are helping address that. And actually, I think the context that he

wrote that in Henry VI was actually to note how important lawyers are.

Part of the change that's happened with GDUFA is we actually -- we used to have only two or three lawyers. We actually have a whole division, and actually an Office of Policy Development, but a whole division of lawyers. So I think we've got probably about 20 lawyers now, just to help address the generic drug issues.

So I think there was, in the past, a lot of confusion about what is available. We can't make all that information available, because it's dependent upon the interactions between the brand and the generic firms and what type of agreements they come to.

But we certainly are watching the patent market a lot more closely, so we're able to act much more quickly, particularly if there are applications in-house when the lawyers tell us that, okay, you can go ahead and approve a product. And that's actually part of one of the process improvements that we've implemented since GDUFA

comes around.

We can't control the cost of it, but we can certainly do our part to effectively monitor the marketplace, and particularly the legal marketplace, that allows applicants to get approval earlier than they might have otherwise.

MR. SCRIBNER: Hi there. Paul Scribner, Aplastic Anemia & MDS Foundation, so bone marrow failure diseases. So I've read articles about drugs manufactured outside the United States, and some of these drugs -- at least in the articles I've read, and I've had patients contact me about similar kinds of concerns -- have very little of the actual active ingredient in them.

I just wonder what the FDA does to ensure these aren't getting into the drug pool in the United States.

CAPT WOO: Great question. I think that's a great concern people have with globalization. So I should share a little bit of my history again. I first came to CDER -- I was in FDA in 2002, but I came to CDER in 2006 to join the Office of

Compliance.

In my first six months there, I put together a slide that demonstrated the shift in manufacturing overseas, particularly China and India, where it had doubled in China and quadrupled in India. And the story I tell is -- that slide was actually used by Dr. Woodcock. And then I was at a DIA conference the next year, and one of the participants from industry actually showed my slide.

So we're absolutely aware of -- you know, so much of the manufacturing occurs overseas. And part of the GDUFA implementation, I'm not going to say it was just with regards to generics, but we've known for years how a lot of that manufacturing has moved overseas.

So even before more recent time, we've created offices overseas, which allow us to get into sites and inspect them more quickly; certainly not as quickly as we might always like, but certainly better than what we were 10 years ago.

There are a lot of changes that are

happening within ORA, the Office of Regulatory Affairs, which has the inspectional component, which is based not only here in the States, but also in areas overseas.

There's a lot going on -- that's probably a whole other talk about international operations -- about how we're trying to improve our ability to respond to manufacturing issues, not just with generics, but also with brand drugs, because certainly a lot of the brand manufacturing has moved overseas as well.

In fact, one of the factors involved in terms of picking where we try to inspect -- used to be we only did domestic sites because that's the only place where we had authority to go in. But now the model that we're using is basically saying, look, it doesn't matter if it's made overseas or here in the States. The risk factors should be the same.

So is it a complex drug? Is it something that goes into the intrathecal space or it has sterility issues that we need to be particularly

concerned about? Is it a complex manufacturing process that really takes some good understanding of setting up a good plant.

Those are the type of questions that we're being asked. So irrespective of whether it's overseas or domestic, we're addressing those issues appropriately. Ad I think it's a good question because, certainly, folks think a lot of the generics are made just in India and China, but certainly a lot of manufacturing for the brands has moved overseas as well.

Other questions, please. These are great. I love it.

(No response.)

CAPT WOO: Okay. Well, thank you very much. And again, I appreciate your time and your engagement here.

(Applause.)

CAPT WOO: Please come to our public meeting on the research agenda. And if you don't, listen in or submit your questions, because we certainly want to hear them. Thank you.

(Applause.)

DR. WHYTE: Thank you, Dr. Woo.

Okay. As I mentioned earlier, at CDER, we work on drugs, but we recognize that folks also have questions about devices. As you remember from that flow chart, there's the Center for Devices and Radiologic Health, which we refer to as CDRH, and I'm delighted to recognize and ask to come to the stage, Kathryn, Katie O'Callaghan, who's the acting senior advisor for Strategic Programs at CDRH.

In this role, she oversees a broad portfolio at CDRH, including a number of strategic partnership and regulatory science programs. Her focus is on directing the center's patient engagement activities and initiatives to advance adoption of patient input as evidence, including patient preferences, which she'll talk a little bit about, and patient-reported outcomes.

She also oversees several other efforts in the center, including the Network of Experts. And we're delighted that we stole, over at CDER, the idea of Network of Experts from Katie and her group

and are implementing it at CDER.

Prior to joining FDA, Katie worked as an R&D engineer for a medtech industry startup. She also served as a research liaison between the University of Pittsburgh Medical Center and MIT Biotech Process Engineering Center.

She studied bioengineering at the University of Pittsburgh with a dual focus in artificial organs and biosystems signals. She also has a BA in German language and literature. Now, that's interesting. See, you can do anything in liberal arts still. People say you can't, but you can.

Katie is also a member of CODETTA. This was our own little research. You didn't give us your fun fact, but we found it anyway, an internationally acclaimed chamber choir. So we'll look forward to music at 1:00 when we resume. But before we take a break, we'll hear from Katie O'Callaghan.

(Applause.)

Presentation – Kathryn O'Callaghan

DR. O'CALLAGHAN: Everything's on the

Internet.

Hi everyone. Good morning. So thanks for the kind invitation and the opportunity to speak with you. I see a lot of familiar faces, so it's nice to be here today.

So as you all know, our newly minted commissioner, Dr. Rob Califf, sees patient engagement as absolutely one of the most critical initiatives for the agency, and this affects all of centers. This is a key component of the President's Precision Medicine Initiative, and really, I think there's a role for patients to play in all of these key initiatives around improving the health of patients across the country and throughout the world.

For those of you who may be a little less familiar with the Center for Devices, we oversee medical devices like pacemakers. You may know someone or you may yourself have a pacemaker, or an artificial knee replacement, or a drug-eluting stent.

We also oversee devices that are very

important in the diagnosis of diseases like MRI machines, blood tests that your physician may order to find out what sort of condition we're working with. And in total, it's over 5,000 different types of medical devices that we oversee and regulate.

Our framework for regulating medical devices includes very simple devices like a tongue depressor to highly complex, robotic surgical suites. We also have low-risk devices like a blood pressure cuff and very high-risk devices that are implanted through open heart surgery and permanently implanted in a patient.

So there's a lot of technical and scientific complexity and regulatory complexity that our engineers and physicians and nurses and epidemiologists are juggling every day. So our center director, Dr. Jeff Shuren, when he arrived in 2009, recognized just how critical it was to keep the laser sharp focus on the patient at the heart of everything we do, so we don't get lost in all of the scientific and technical complexity in

the rapid pace of evolution of technology.

Our vision is that patients in the United States have access to high quality, safe and effective medical devices of public health importance first in the world.

In January, we released our strategic priorities for the 2016-17 period. We've identified three top priorities for the center, and this is a priority for all of the over 1700 employees in the center. And one of those three is to partner more closely with patients.

We recognize -- and this is true of Jeff and his senior leadership team, all of our office directors and dozens of programs and divisions across the center, we recognize that in order to truly be successful in our mission in service of patients, we need to interact more regularly, more routinely with patients as partners and work together.

So ultimately, our vision is oriented at patient-centered device innovation and evaluation. These are just a listing of some of the initiatives

we have ongoing. Patient preferences is something you may have heard a little bit about. There have been some patient preference studies in the device space, as well as in the drug arena.

We did a case study on obesity and weight loss devices several years ago, which was the cornerstone for our policy, which we issued last May in draft. We'll be finalizing that this year, which really talks about how we can get the patient's view on benefit-risk. Do the benefits outweigh the risks? Are patients willing to tolerate different levels of risk with different levels of disease severity and depending on whether or not it's an unmet need condition?

We also partnered with the Medical Device Innovation Consortium, which is a public-private partnership that includes industry, government, non-profits patient groups on a framework for how patients can -- patient perspective on the patient-centered, benefit-risk framework can really reorient how we look at these questions.

Clinical studies is the next frontier. I

think there's a lot of great work that we can draw upon. For the device center, we have a benefit-risk framework that's out for clinical trials. That's our IDE, our version of the IND.

We're looking to include patient input on clinical trials in terms of ways to reduce barriers to patient participation, improve recruitment and retention, and make sure that we're actually considering what are the important questions to patients; which outcomes matters most to them, are we studying those.

Patient-reported outcomes is something I think many of you know quite a bit about, and this is something we are putting focus on in the center over the next two years.

You may also have heard about our Patient Engagement Advisory Committee, which we announced that we were establishing last September. Our advisory committees, as many of you know, have patient representatives that sit on those committees. But we also recognize that there is an opportunity to have a more fundamental and

comprehensive discussion with patients that represent a variety of perspectives on how we can think about including patient input across the total product lifecycle and throughout all of the functions that we do here at FDA.

Part of our strategic priorities include targets for us to increase the direct interactions between our staff and patients, so that they can all better understand the patients that they serve and that are affected by the decisions we make every day.

This is our schematic of how a medical device is conceived of, invented, built, tested, evaluated from a regulatory perspective, and ultimately, if determined to be safe and effective, launched onto the market and studied as it rolls out into the real world.

I may be retitling this slide. Our director, Jeff Shuren, has really encouraged us to think about different ways that we can motivate an army of patient scientists to take part in reshaping this landscape. So I think there are a

lot of different places throughout.

A lot of this was informed by a workshop we had in September 2013, and the answer was patient perspective can be incorporated from soup to nuts. These are a couple of the big impact areas that we're focusing on, and very much encourage you all and challenge you all to think about whether or not any of these are areas that you and your patient communities that you serve would like to get involved.

This is just a snapshot of the huge increase in patient perspective data that we are seeing in regulatory submissions. So this is patient-reported outcome data that we saw in device regulatory applications. Half of our PMAs, that's the high-risk device category that we received last fiscal year, included patient-reported outcomes as a primary or secondary endpoint. So this is a significant chunk of the pie.

We've seen a huge spike, an over 500 percent increase in submissions since 2008, which was the year before the agency released guidance on

patient-reported outcomes and just quite a huge number.

So ultimately, the goal of all of this and all of our activities across the agency and elsewhere is to improve patient health. But we're doing this not only by studying patients, but by interacting with them and better understanding their experiences, their needs, and their preferences.

I sort of look at this as two major spheres of activity. One is the art of patient engagement and the other is the science of patient input, and both are critically important. They're like two sides of a coin. You really can't have one without the other.

But within the science arena, this is really important, because we have to look at valid scientific evidence in support of our decisions. So the work that we're doing in patient-reported outcomes and patient preferences really does anchor the outputs of patient engagement with rigorous methodologic science.

So thank you for your attention, and I'm happy to take any questions.

(Applause.)

DR. WHYTE: Well thank you, Katie.

At this point, we are going to take a lunch break until 1:00. Remember, color codes on your desks. So when we get back at 1:00, I'm going to need a volunteer from each of the colored teams to play Jeopardy, and people are going to be excited and have fun, and it's going to be great. So I'll see you all at 1:00. Thank you.

(Whereupon, at 11:42 a.m., a lunch recess was taken.)

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

(1:00 p.m.)

Jeopardy

DR. WHYTE: All right, people. Let's get excited about playing Jeopardy.

(Applause.)

DR. WHYTE: There we go. Where are my clappers?

(Applause.)

DR. WHYTE: All right. We have four teams, I believe, and there's four colors, and we're supposed to have a representative from each team, each table.

All right. Laurie Haughey, we have different colors. Am I supposed to say -- okay, I'm going to let Laurie Haughey explain a little, and then I'm going to come back.

MS. HAUGHEY: Okay. Every table has one of those. Hold it up, John. Everyone knows. Okay. There are four colors. There are four teams. Every table needs to nominate a volunteer. I think I've talked to most of you. So that volunteer can

come up front.

There are four people on each team. So if you don't know the answer, don't worry, we don't know that it's not you who knows the answer. It's not Family Feud style, but it sort of is.

One person from each team can sit and be captain. They have a buzzer. Three people can stand behind them. They need help. Come on, guys; one from each table.

DR. WHYTE: This is Jeopardy meets Family Feud.

(Pause.)

DR. WHYTE: We should have this on video. Okay.

All right. Well, before we start, let's have everyone, at least the team lead, seated at the table, tell us who they are. So we'll start closest to me with Team 1.

TEAM 1: Hi. Rob Goldsmith with the Cancer Support Community.

TEAM 2: Diane Dorman.

TEAM 3: Paul Scribner with Aplastic Anemia

& MDS Foundation.

TEAM 4: Megan O'Boyle with Phelan-McDermid Syndrome Foundation.

DR. WHYTE: Okay. Are we loaded, ready to go? All right. Since we don't have a returning champion, the computer will randomly select who will start first. And there you see your categories: Speed it Up, Acronym Soup, Trials and Tribulations, Play it Safe, Picture This.

So the rules are a little different than the regular Jeopardy. Team 1 wins; they get to pick. But in order to activate your buzzer, the buzzers won't be activated until I read the whole question. So you actually can't chime in until I finish the question. Then you'll click, and the computer will tell me if you clicked it properly.

Those are those the rules? I believe that's the case. So are you ready to play Jeopardy?

TEAM 1: Ready.

DR. WHYTE: Let's have some enthusiasm, everyone. All right.

(Applause.)

DR. WHYTE: let's start with Team 1.

TEAM 1: So we'll take Play it Safe for 300.

DR. WHYTE: Okay. This might accompany the approval of a drug with known safety issues. Remember, give your answer in the form of a question?

TEAM 2: REMS.

DR. WHYTE: In the form of a question, Diane.

(Laughter.)

TEAM 2: What is a REMS?

DR. WHYTE: What is a REMS is correct. It could also be a MedGuide.

All right. And feel free to confer with your colleagues as well. Remember, it's part Family Feud. Team 2, select.

TEAM 2: Acronym Soup for 300.

DR. WHYTE: NME.

TEAM 2: New molecular entity.

DR. WHYTE: Okay, you have to buzz in. No one has buzzed in. We can't count it.

TEAM 2: What is a new molecular entity?

DR. WHYTE: Tell me your answer again.

TEAM 2: What is a new molecular entity?

DR. WHYTE: What is a new molecular entity? That is correct.

All right other teams. Wake up. Team 2, choose again.

TEAM 2: Acronym Soup for 400.

DR. WHYTE: Acronym Soup for 400. NDA.

TEAM 3: New --

DR. WHYTE: In the form of a question.

TEAM 3: What is a new drug application?

DR. WHYTE: What is a new drug application is correct. Very good. Team 3's on the board. Choose again.

TEAM 3: Trials and tribulations for 400.

DR. WHYTE: Trials and tribulations -- the major submission officially requesting drug approval?

TEAM 1: What is an IND?

DR. WHYTE: What is an IND is incorrect.

TEAM 3: What is an NDA?

DR. WHYTE: What is an NDA is correct.

Team 3. Okay.

TEAM 3: Play it Safe for 400.

DR. WHYTE: Okay. Play it Safe for 400. The FDA collects reports on adverse events through any of these systems. You only need to name one.

Team 2?

TEAM 2: What is Sentinel and what is MedWatch?

DR. WHYTE: What is Sentinel and what is MedWatch. They're both acceptable, and so is FAERS or VAERS. Very good.

Okay. Team 2, choose again.

TEAM 2: Play it Safe for 200.

DR. WHYTE: Play it Safe for 200. The responsible party legally required to report known adverse events.

TEAM 2: The patient themselves.

DR. WHYTE: Say that again.

TEAM 2: Who is the patient? What is the patient?

DR. WHYTE: That is incorrect.

TEAM 1: Who is the healthcare provider?

DR. WHYTE: Who is the healthcare provider? That is incorrect as well.

TEAM 4: What is the industrial partner or the pharmaceutical company?

DR. WHYTE: That is correct. What is industry? I'll accept that.

I know, Team 3, it looked like you're going to buzz. You'll have to put your protest later.

Okay, Team 4, you can select.

(Laughter.)

TEAM 4: Acronym Soup for 100 please?

DR. WHYTE: Acronym Soup for 100. CDER.

TEAM 2: Center for Drug Evaluation Research, what is the Center for --

DR. WHYTE: Very good. What is the Center for Drug Evaluation and Research.

(Applause.)

DR. WHYTE: Okay. It's close, except Team 1's negative. Okay. Choose again. Team 2 gets to choose. Diane?

TEAM 2: Picture This for 100.

DR. WHYTE: These pictures are tiny; I'm

warning you.

(Laughter.)

DR. WHYTE: Put your glasses on.

TEAM 1: What is a physician's insert?

DR. WHYTE: I'm going to accept that. It's what is the label? But we sometimes refer to it as prescribing information, package insert. It's close and it's small, so we'll accept it. And you guys are in the negative. All right.

(Laughter.)

DR. WHYTE: Team 1, choose again.

UNIDENTIFIED SPEAKER: Can we have bigger pictures please?

DR. WHYTE: There's no bigger pictures. That's a warning.

TEAM 1: Speed it Up for 500.

DR. WHYTE: That's good. Speed it Up for 500. In 2015, almost half of the new drugs approved were to treat this category of disease. Team 2?

TEAM 2: What is a rare disease?

DR. WHYTE: What are rare diseases? That is

correct. You clicked too early, and I allowed it.

TEAM 1: What is a rare disease?

(Laughter.)

(Applause.)

DR. WHYTE: I mean, those are the rules. Diane, I knew that you'd know the answer to that, but that shows you, you have to follow our rules. And if you don't follow our rules, there's penalties. So you've got to click.

So I'm sorry, I was in error, but good work Team 1, though you're at zero.

(Laughter.)

DR. WHYTE: Go ahead.

TEAM 1: We'll go with Acronym Soup for 500, please?

DR. WHYTE: Acronym Soup for 500. REMS.

TEAM 2: What is Risk Evaluation Mitigation Strategies?

DR. WHYTE: Very good. What is a Risk Evaluation and Mitigation Strategy.

(Applause.)

DR. WHYTE: Team 2, choose again. Okay,

stop resting on your laurels. Team 2, choose again.

TEAM 2: Which one?

UNIDENTIFIED SPEAKER: Not pictures.

TEAM 2: Yeah, not pictures. Acronym Soup, 200.

DR. WHYTE: Acronym Soup for 200. IND. It's a question, but we'll take it. Team 4.

TEAM 4: What is investigator --

DR. WHYTE: Got to be correct.

TEAM 4: -- new drugs.

DR. WHYTE: Say it again?

TEAM 4: Investigational new drug.

DR. WHYTE: What is investigational new drug? In the form of a question. I'll give it to you Team 4. Okay.

TEAM 4: Thank you.

DR. WHYTE: Okay. What is an investigational new drug, not investigator, but you came around. All right.

Choose again, Team 4.

TEAM 4: Speed it Up for 300.

DR. WHYTE: Speed it Up for 300. The FDA has this number of expedited drug approval pathways.

TEAM 4: Four, what are four?

DR. WHYTE: What are four? That's correct. That's correct. Sixty percent of drugs last year, remember, used at least one of these pathways. I know it was early in the morning, so I'm glad you paid attention.

Choose again Team 4. You're coming up. Tying up.

TEAM 4: Speed it Up for 400 please.

DR. WHYTE: Speed it Up for 400. A drug granted accelerated approval is required to conduct this after approval. You've got to wait until the end of the question.

Okay. Team 2? Oh, no -- yes, Team 2.

TEAM 2: Postmarketing study. What is a postmarketing study.

DR. WHYTE: Excellent. What is a postmarket study or trial? Very good.

Okay, Team 2, choose again.

TEAM 2: Speed it Up for 100.

DR. WHYTE: Speed it Up for 100. Two-thirds of novel new drugs last year were first approved in this country.

TEAM 2: What is the United States?

DR. WHYTE: Yes. Okay. What is the United States? Excellent.

So remember, you have to wait until the end of the question for you to register. I've got a lot of quick people up here. Okay. Team 2 again.

TEAM 2: Speed it Up for 200.

DR. WHYTE: Speed it Up for 200. This designation leads to a six-month review clock.

TEAM 4: What is fast track?

DR. WHYTE: No, that's not correct.

TEAM 2: What is breakthrough therapy?

DR. WHYTE: That is not correct.

TEAM 3: What is accelerated review?

DR. WHYTE: That is not correct. What is accelerated approval.

TEAM 3: What is priority review?

DR. WHYTE: What is priority review is

correct.

(Applause.)

DR. WHYTE: All right, Team 3.

TEAM 3: Trials and Tribulations for 500.

DR. WHYTE: Trials and Tribulations for 500, also known as compassionate use.

TEAM 3: What is expanded access?

DR. WHYTE: What is expanded access is correct.

(Applause.)

DR. WHYTE: Wow, Team 3 and Team 2 are neck-and-neck. Team 1, let's get on the board. Okay. Team 3, let's choose.

TEAM 1: We're trying.

TEAM 3: Play it Safe for 500.

DR. WHYTE: Play it Safe for 500. This is going to be a tough one. These standards ensure the drugs you buy online are FDA compliant.

TEAM 4: What are online standards?

(Laughter.)

DR. WHYTE: No. I'd like to give you credit for trying, but no.

That amount of time on the bottom. Come on, someone, chime in. Okay. The answer is what are VIPPS? The verified internet pharmacy practice sites.

All right. So Team 4 chooses again, correct? No. Team 3. Excuse me. Team 3 you choose again.

TEAM 3: Picture this for 400.

DR. WHYTE: Okay. Get your glasses.

TEAM 2: Is that a patient insert?

DR. WHYTE: No, I'm sorry. It's not a -- okay.

TEAM 1: What is the Federal Register?

DR. WHYTE: What is the Federal Register notice is correct. Excellent. You choose again.

TEAM 1: Let's do Picture This for 200.

DR. WHYTE: Picture This for 200. Okay. I want you to look at the arrow that's pointing to a box.

TEAM 3: What is a black box warning?

DR. WHYTE: What is a black box warning is -- is a black box warning good enough? Correct.

Excellent.

All right. Team 3 is now in the lead. Choose again.

TEAM 3: Picture This for 500.

DR. WHYTE: All right. Picture This for 500.

TEAM 4: What is the drug label?

DR. WHYTE: This one is not going to be the drug label, no.

TEAM 2: What is the drug label?

DR. WHYTE: I'm not going to give you that, drug label. We still have a little more time until that little icon at the bottom goes. I know it's hard to see.

TEAM 3: What is patient use instructions?

DR. WHYTE: No. No. It's actually over-the-counter drug facts label. That's a tough one. All right.

Which team is in control of the board? I forget. Team 3.

TEAM 3: Trials and Tribulations for 300.

DR. WHYTE: Trials and Tribulations for 300.

This needs to be submitted to the FDA before the drug can be tested in humans. You have to wait until the end of the question.

TEAM 3: What is an IND?

DR. WHYTE: What is an IND is correct. Thank you.

Okay. Anyone could still win probably, except Team 4.

(Laughter.)

DR. WHYTE: But that doesn't mean you shouldn't try. Okay. Team 3 choose again.

TEAM 3: Trials and Tribulations for 200.

DR. WHYTE: Trials and Tribulations for 200. This phase trial is typically the final phase before approval.

TEAM 3: What is a phase 3 clinical trial?

DR. WHYTE: What is a phase 3 clinical trial is correct. Very good.

Team 1 you would be doing well if you just wait until the question was over.

(Laughter.)

DR. WHYTE: Okay. Team 3, choose again.

TEAM 3: Picture This for 300.

DR. WHYTE: Picture This for 300.

TEAM 4: Who is Janet Woodcock?

DR. WHYTE: Who is Janet Woodcock is correct. Thank you.

(Applause.)

DR. WHYTE: Okay. Two left. Team 4 is in control.

TEAM 4: Play it Safe for 100, please?

DR. WHYTE: Play it Safe for 100. In approving drugs, FDA conducts a risk and blank analysis.

TEAM 4: What is benefit?

DR. WHYTE: Benefit is correct. What is benefit?

TEAM 4: Almost zero.

(Laughter.)

DR. WHYTE: Okay, and our last question.

TEAM 4: Trials and Tribulations --

DR. WHYTE: Chance of a new compound becoming an approved drug is 1 in?

TEAM 2: What is 1 in 10?

DR. WHYTE: Oh, that would be nice. No, it's not 1 in 10.

TEAM 4: One in 10,000. What is 1 in 10,000?

DR. WHYTE: It is not 1 in 10,000.

UNIDENTIFIED SPEAKER: What is 1 in 200?

(Laughter.)

TEAM 1: What is 1 in 100?

DR. WHYTE: It is not 1 in 100.

TEAM 3: What is 1 in 1000?

DR. WHYTE: It is not 1 in 1000. It is 1 in 5000.

I want to congratulate all of you, but especially Team 3. Where are you? Congratulations.

(Applause.)

DR. WHYTE: There are no prizes except bragging rights, which should count as something. Someone should tweet it out that you won Jeopardy at FDA.

Okay. I don't know if Brian Hasselbalch has left. I think he's still here.

All right. So we were going to having a quiz, a clicker question. Maybe we should skip it. They might be tired. I don't know. All right. We'll ask it still.

True or False. It is legal to buy prescription drugs online. I know you're tired of questions, but here's a chance to redeem yourself. Okay. I think there's a couple more people we're waiting for.

(Audience polled.)

DR. WHYTE: All right. The correct answer is true, and we're going to hear a little more about this.

At this time I'm going to introduce Brian Hasselbalch, who is the deputy director of the Office of Policy for Pharmaceutical Quality. He began his service with FDA as investigator and performed primarily drug process inspections and related investigations in California and overseas.

He transferred to compliance office at FDA in the mid-90s, where he reviewed regulatory cases in the area of drugs, cGMP. He drafted guidance

policies and regulations relating to cGMP for drugs. And as I mentioned, he's now the deputy director for the Office of Policy for the Office of Pharmaceutical Quality.

His fun fact is that he participated in the Peace Corps and was stationed in Thailand. So with that, Brian Hasselbalch.

(Applause.)

Presentation – Brian Hasselbalch

MR. HASSELBALCH: Thank you, John. And, Hank, thank you very much for that photo.

(Laughter.)

MR. HASSELBALCH: It would not have been my choice, but thank you for looking on Google.

All right. Wow. I get to follow Jeopardy. How many people get to do that in their careers? I hope never again. But you guys are at least energized. I hope what I have to say is useful and interesting, and I understand there will be time to address questions later. But if something comes up and it's burning, and you want to ask it right away, just shoot your hand up and interrupt me.

I'm okay with that.

I will go through some slides kind of quickly. I'll give you a framework for how we regulate drug quality and, therefore, drug safety with respect to manufacturing risk and controls. But I want you to understand that there's a host of orchestrated activities that are undertaken by FDA worldwide to ensure drug quality to U.S. consumers.

It begins with a solid policy foundation, both with a combination of regulations and recommendations that I'll go over. And a big part of what we do is review applications for marketing approval. And in that, we look at detailed content about its production and control.

We also conduct a number of types of site inspections. We also test samples of drug products and APIs in commerce. And we listen carefully to feedback from the marketplace, both from the industry and patients and consumers.

Let me go into that in a bit more detail. We have a set of regulations that govern quality, and I'll describe those a little bit later. But

their acronym is cGMP, current good manufacturing practices. And we also have regulations that describe in detail the content required in a marketing application that describe the chemistry and manufacturing controls for the drug substance or the API and the finished product.

USP, the Pharmacopeia, including USP and the Homeopathic Pharmacopeia of the United States, also play an important role in assuring quality, particularly for OTC products that aren't necessarily subject to an application review process.

You know, I had links. Hank, can I click on a link here?

(Pause.)

MR. HASSELBALCH: That's okay. We're safe. It's the government system. Can't be hacked. That's not actually funny anymore.

(Laughter.)

MR. HASSELBALCH: We jumped ahead a bit. I wanted to show you and please leave it here -- this is fine -- often on a drug label you'll see the

drug name, comma, USP. You may not see it. Whether it's on the label or not, if the name is recognized in the USP, the United States Pharmacopeia, the drug, while in commerce has to conform to that.

There are exceptions to that; they're rare. But generally speaking, that's the role that U.S. plays. It acts as a referee for standards or specifications for drug quality for drugs commonly used in the market. Doesn't operate much for innovators; just the drugs that are generic or OTC monograph stage.

We also issue recommendations, mostly the industry, and mostly in the form of what we call guidance for industry. Here's a guidance that we just published last year. It was directed toward generic producers, and it recommended that they better match the size, shape, and other characteristics of the dosage form to the innovators, so that we didn't have a generic tablet that was twice the size or dimensions of the innovators and could be harmful when swallowed or

cause concerns when being used.

We also conduct a fair amount of outreach, both in the regulation and guidance drafting phase, and we do a fair amount of outreach after we finalize the new regulation or revised or finalized a new guidance.

The outreach we conduct also involves partners with key stakeholders in the industry. There are a number of trade organizations that we partner with in reaching out to manufacturers primarily, but also in some cases to other groups.

As you've learned, we look at all -- I'm sorry, many drugs have to have a new drug application submitted or an abbreviated or a biologic license application, but some premarket application is generally submitted for most drugs in commerce, not all.

The OTC monograph system that FDA manages is an exception to the application-based rule for approval, and OTC monographs cover things like aspirin tablets, antiperspirants, sunscreen, and a number of other products like that, or various

common cough/cold products, mentholated cough drops and so on.

They are not the subject of an approved application. However, virtually all other drugs you could think of, including over-the-counter drugs like ibuprofen, naproxen, and even nicotine patches are the subject of approved applications to be legally marketed.

We spend a great deal of effort in the application review side. In fact, in the Center for Drugs, I would say that much of our capacity and scientific expertise is applied toward the pre-market phase of a life cycle of a drug.

In the quality area, nonetheless true, and later I'll show you some additional information about that. But there's a massive effort undertaken during the pre-market cycle in a constrained window of time to look over very carefully all the content in what we call the chemistry and manufacturing control section of a new drug or an abbreviated application, or even a biologics license application.

We do a pre-market review for original applications, but we also review changes proposed or affected after approval has been granted. So certain changes require a reapplication, if you will, to the agency. That triggers another round of scientific reviews of that change to make sure it doesn't raise concerns or challenge the bioequivalence or bioavailability of the product, and preserves its quality as it did when originally approved.

A number of other changes we allow to be made without pre-market refereeing, and we often hear about those either through a supplement called the changes being affected supplement or an annual report.

We're doing some publicly announced policy work with regulatory partners worldwide actually to reduce the amount of supplementation we get after original approval that requires a pre-market review; in other words, preferring to cover that mostly in a postmarket setting, if you will, where the change is affected based on a foundation of

regulation or guidance that likely won't harm the efficacy of the drug or the safety of the drug. We look at it near term to its implementation by the company, and we hope that that will free up innovation.

We do also look at manufacturing facilities. We look at them wherever they are in the world, if they're providing the active ingredient, or the finished product to a U.S. market. We inspect over a thousand facilities, unique facilities, every year. We do maybe 1500 to 1700 different kinds of inspections in that year, sometimes a repeat visit to the same site.

We conduct an inspection of a facility that's brand new to making drugs before we grant approval of the marketing application. And we do that as part of the review cycle. It's one of the review disciplines, the facility evaluation. There's a headquarter-based paper review, if you will, and then accompanied by an onsite inspection.

Primarily the inspection for pre-approval purposes is to verify that the application's

content is accurate, and that the facility is actually capable of integrating that new product, pending approval into the existing operation safely and correctly without any risk to cross-contamination.

We also conduct surveillance inspections, and these are inspections that happen periodically throughout the life of a facility and a product. The frequency varies by risk. We have a risk model that picks the facilities every year that we go to, and that model is agnostic, if you will, with respect to whether it's foreign or domestic.

That really bears on the nature of the product or drug being made and the control strategy around it and perceptions by experts of the risk associated with that, along with other information or data we have learned or gleaned about that facility from other sources in the past period of time.

A big part of our inspection capacity is used by periodic surveillance inspections. These happen, whether it's OTC or Rx. They happen

whether it's an application or non-application product. We also do a for-cause or directed inspections when, as the name implies, a cause arises.

A complaint pattern of adverse events suggesting a defect or quality problem might trigger one of these for-cause inspections, and there are other reasons. We hear a lot from informants about quality problems at facilities that will often trigger a site inspection.

We test samples of product in commerce, finished product, the active ingredient. Only infrequently do we take an inactive ingredient sample. An inactive is also known as an excipient. It's the other things in a drug dosage form that help deliver the API to the targeted tissue and give you something to hold or handle that's large enough to use.

Much of our sampling is of finished products in commerce. We don't test for every attribute of the finished product, but we test all the key attributes. And we generally focus the testing to

those characteristics or attributes that we think are at risk to failing or being a problem for patients.

So we might check how fast it dissolves or releases the active ingredient out of the dosage form, or we might check for purity or levels of impurities. And of course, some years ago, we looked extensively at heparin in commerce to make sure it was free of a known impurity that caused death and injury to U.S. consumers.

As I mentioned, we listen carefully to the market. By that I mean that we're constantly surveying and evaluating information we gain from both companies and consumers and caregivers. Certain applicant holders have to report defects of products or batches that they put into commerce, whether or not they recall, and often their report of a defect leads to a voluntary recall.

We also look carefully at MedWatch reports. MedWatch reports, as you've learned, are about reporting for adverse events. They're obligatory for applicant holders and sponsors, but anybody can

report through MedWatch, any concern or complaint about a product.

We get thousands of those a year that are thought due -- not confirmed usually, but thought due -- to a quality problem. Decreased therapeutic effectiveness, some visible defect in the product that's noticed by the patient or the caregiver often triggers or can trigger a MedWatch report.

That report gets reviewed by one office. If it's deemed to be quality related or thought quality related, it gets sent on to another office that is dedicated to looking at a host of this information bearing on quality, recalls, defects, and so on, as well as consolidated consumer complaints.

A separate system that is managed by our Office of Regulatory Affairs, the inspectorate. But all of this is brought together by a team in one office that looks at this and decides, is there a pattern, a trend, or a real problem that warrants some reaction or response by the agency.

Then, if we see a need to follow-up, from

the information we've looked at, we often may call the firm. We may send an investigator out to visit them and collect additional information. And it may, as I said earlier, lead to a voluntary recall.

We don't have the authority to order a recall for a human drug, but we certainly monitor recalls when they happen, and we're informed of them. We have a system for making sure that the recall scope is appropriate.

We keep an eye on shortages. We're obligated to consider shortage potential in deciding whether we encourage or discourage a recall and in our response, in any case, to any quality defect.

We also have arrangements with partners, other regulatory agencies around the world, to share information about quality problems. We have a Rapid Alert Notification System among which dozens of countries participate and share information, for example, about recalls that may occur in their market that they think could impact somebody else's.

So that summarizes the picture, if you will, of how we regulate quality. I'll go into a little bit more detail. What I haven't talked about yet is what we do if see a quality problem in terms of enforcement. We have some enforcement capacity at FDA. We have the authority to deny approval of a marketed product or an application pending approval.

We also have the authority to withdraw approval if they can't correct or maintain quality to a sufficient standard. We rarely see a need to withdraw approval once granted, but that's an option.

Following a site inspection, we can issue a warning letter, which is a caution to the company to fix or else further action may be taken, and quite often, that results in corrective actions. When it doesn't or when a warning isn't sufficient to resolve the risk, we might seize product or we might issue an import alert and block entry for a foreign produced good entering the U.S. directly, or we might seek an injunction.

A seizure and injunction are not easy things to do. They require the participation of the Department of Justice and a court, whereas an import alert is something that we can do administratively within FDA. We don't need to go to a judge and seek permission for that. And of course, approvals, denials, and grants are administrative actions we take within FDA.

Surveillance testing and any feedback we get from the marketplace or companies often can result in one of these actions, if what we're seeing in the response to the defect isn't sufficient, either in a timely way or we think that the company isn't really solving the root cause of the problem that led to that defect.

There are a lot of companies involved in the supply chain of drugs, both from the drug substance or the active ingredient side -- those terms are synonymous, by the way -- through all the finished product to the consumer and retail pharmacies and outlets. We don't inspect all of them, but we do inspect key players. Anybody who makes a dosage

form, we inspect. Whether it's OTC or Rx, foreign or domestic, we inspect them if it's in the U.S. market, legally.

We also inspect the active ingredient sites, and we inspect sites that do contract work for any one of those. There are sterilizing sites that specialize only in certain types of sterilization. We inspect them. Contract laboratories are often used for unique or specialized testing or simply to help capacity with the manufacturing site. We inspect them if they're doing it to satisfy the quality control of the drug.

We also inspect packaging sites. Most of the drugs that we take that are in blister packs are produced by specialized repacking facilities. We inspect them, and we inspect others who may take large -count bottles and sub-divide them into smaller-count bottles for patient use.

We inspect a certain type of pharmacy compounding operation, as a result of congressional legislation passed a couple of years ago. They're known as outsourcing facilities, sometimes referred

to as 503B, which is a reference to the congressional act that gave us the authority to inspect and regulate them more like, not equivalent to, but more like commercial manufacturers.

I think there are about 53, by last count, registered today. They've all been inspected, I believe, and we're actively regulating that activity. We have interim guidance for them now, and we'll soon pursue a new regulation dedicated to outsourcing facility production activities, many of which, by the way, are sterile drugs.

Drugs made in the U.S. only for export, there are very few of them, but there are some. They're subject to the same inspection and oversight regime. And occasionally, we inspect clinical trial sites. For those clinical trial materials that are produced by a facility that isn't already making a commercial drug, they generally don't get inspected unless the IND reviewer or some other information suggests a need to do that. We also don't routinely inspect inactive ingredient producers or container closure

manufacturers, although we have when problems occur and we'll continue to do that.

I mentioned we've got this massive bureaucracy over the review of drug applications. I don't think I used the word "massive," but it's big. And I don't say that in a begrudging sort of a way, part of it.

We have, in the last year, instituted a new way to review the quality portions of a new drug application, or abbreviated application, or BLA. We have what we call an integrated quality assessment team, IQA team, that has all the disciplines you see here that come together and not literally at a table, but they review each of their subparts of the application. Then they come together as a team and discuss and decide what the recommendation to the Office of New Drugs or Office of Generic Drugs should be, who renders the final approval or not decision for the center and agency.

You can see there's a host of experts that are involved. I would say in the past, you might have seen a few of these involved to be sure, but

not the same group. For example, we have more microbiologists now looking at non-sterile drug applications to assure bioburden reduction and appropriate limits on any microbial contamination that might exist in the facility and impact the product, even though it's a non-sterile product. So we're doing more of that than we did before.

We have teams in the center now, paying more attention to the facility design and control strategy, including testing methods, than we did before. Each of these are more specialized, being allowed to be more specialized in their area. That does add effort, but we're still doing this within the constrained window of time we have under the user fee arrangements, generally a 10-month clock to decide on an application.

I mentioned the cGMP regulations. Here they are. They're published in the Code of Federal Regulations, and there are these subparts. I will not read them to you or go over them each in detail. Time doesn't permit and probably your interest isn't so great as to warrant that.

But suffice it to say that GMP regulations have at their core principle, the idea that quality has to be designed and controlled in the finished product. It can't simply be verified by testing in product alone.

You've probably heard this said a number of times. Quality is a function of its production and control strategy; that is the controls given, the raw materials used, the method of processing those raw materials to create a final dosage form and all the procedural controls and governance activities that go on in a facility to make sure that final product that you and I take is what it was intended and designed to be, every day, every batch, all year long.

Remember, we're not taking the drugs that are being tested. Testing generally destroys the drugs. The drugs we take ought to be like the drugs tested, and the tested drugs ought to be representative of the ones consumers use and rely on.

So there's limited testing of any final

product. It has to be based on other assurances of quality before testing is started. So the GMP regulations, here, I've displayed for 211, which cover finished pharmaceuticals.

There is another set of GMP regulations at 21 CFR 212 that covers positron emission tomography drugs, and then there are others that cover different kinds of animal medicated feeds, not of interest here, and another body of regulations for certain biologics, including some of the ones CDER regulates, monoclonal antibodies and therapeutic proteins.

Now finally, I've saved the last slide for the organizational propaganda, if you will. I mentioned that massive effort on the CMC or the chemistry manufacturing control side and the quality side, we have founded in CDER a new Office of Pharmaceutical Quality, effective this past year. I hope you can help us be faithful to our mission and vision.

That wraps up my presentation. I hope you found that useful.

(Applause.)

DR. WHYTE: I think we have time for one or two questions if anyone wants to come to the mic or do we have any questions online?

(No response.)

DR. WHYTE: All right. Well thank you. They're tired from Jeopardy.

MR. HASSELBALCH: Yes.

DR. WHYTE: Thank you.

So I am going to ask one more clicker question, so get your clickers ready. It's a true or false question. And true or false, your healthcare provider is required to report any serious adverse events from a drug to the FDA. A is true and B is false.

I see a lot of people not clicking. A 50 percent chance of being right.

(Audience polled.)

DR. WHYTE: All right. The correct answer is false, but clearly we have a little bit to learn. The healthcare providers are not required to report serious adverse events.

We're now going to hear from my good friend and colleague, Captain Catherine Chew, who's the deputy director of the Division of Drug Information here at CDER. Captain Chew, as I mentioned, is the deputy director of the FDA's Division of Drug Information, which responds to inquiries from industry, healthcare professionals, and consumers from within the U.S. and internationally.

Some of you may know, we have a call center, which Captain Chew helps oversee. As part of the FDA drug information team, she also oversees our social media accounts including Twitter, Facebook, and the listserv outreach. So if we haven't responded to your tweet or your Facebook comment, Cat is the person to talk to.

You may also recognize her, as she is the voice and face for many of our audio and video podcasts. So without further ado, my good friend and colleague, Captain Catherine Chew.

(Applause.)

Presentation – Catherine Chew

CAPT CHEW: John just outs me with things,

but that's what good friends do, right?

Thank you, John, and I'm happy for this opportunity to present here, and I had actually submitted a fun fact. And since it wasn't read, I'm going to say it here, because that's what patients do, right? And that's what patient advocates do. We shamelessly take every opportunity to put in a plug for our disease.

I have a disease called moyamoya. It's a very rare disease where my carotid artery cuts off, and it can lead to death if it's not taken care of. So go home, read about moyamoya disease, and I've done my duty for today.

All right, now to the FDA part. I'm glad to be here as a patient and to represent FDA today, and I will talk about these three things here. We've heard a lot about MedWatch already from Hank in the morning, and then Jason Woo, and from Brian just now. So I will tell you exactly how to report adverse events through MedWatch.

Then, as you give us this information in, we report this information back out to you through

various drug information tools, so we'll go over that. And finally, we will talk about how you can engage with CDER in different ways. We've heard about many touch points already today, and I will tell you how you can interact with us in the Division of Drug Information.

DDI is part of our Office of Communications, and we are the CDER focal point for public inquiries. We heard today, if you have a generic question, you can email OGD. If you have a question about the drug shortages, you can contact Val Jensen. If you have a product quality problem, you can contact Brian. But if you have no idea where to start, you can contact us.

In DDI this past year, we responded to 48,000 calls, 16,000 emails, and 1,000 letters. So you've kept us busy. We have three main phone lines. We have our drug information line, we have our small business and industry assistance line, and then we have our MedWatch line. So I'm going to talk about how to report to MedWatch.

Just out of curiosity, how many people here

take a prescription?

(Show of hands.)

CAPT CHEW: All right. The next time, take your prescription bottle, there's a phone number on that bottle. That's the MedWatch number. So if you call it, you'll get us. So call us.

All right, MedWatch. MedWatch was established in 1993, and you've heard a lot about it already today. The goal is for you to report adverse reactions in to us here at FDA. Then we take that information, we do a lot of investigation, a lot of digging to see if there is a real safety issue. And if there is, then we send that safety information back out to you.

OHCA, our Office of Health and Constituent Affairs, they like to say that 20 years ago, MedWatch was all about reporting in, but now we have all done a great effort in sending this information back out to you.

So why should you report? And Hank did a great presentation telling about clinical trials and the drug approval process, and we know that

that clinical trial period is very small. The period is very short; the population is very small, usually a couple hundred to a couple thousand patients.

So let's say there's a very rare side effect such as drug-induced liver toxicity, which shows up in 1 in 10,000 patients. But our clinical trial was only 3,000 patients, so this adverse reaction may never show up during clinical trials.

Also, clinical trials have very narrow populations. We often exclude pediatrics, the elderly, those with renal or liver problems, and so it's a very small population. We have narrow indications that are studied in clinical trials.

We don't study this indication plus diabetes, this indication plus heart disease; it's a very narrow population. And again, this is short duration. So drug trials are usually from a couple weeks to a couple months, so a lot of the side effects don't come out until it's actually on the market.

The safety of a drug really develops over

months and years after it has been on the market. When you hear about these side effects and you experience it, you report it to us, then we can do efficient postmarketing monitoring. Then, we can catch those low frequency reactions such as the liver toxicity, or then we can look at more information with these high-risk groups, such as pregnant women, women who are nursing, the elderly, those that are at high risk for certain complications.

We can then look at long-term effects. For example, lipodystrophy in HIV meds, occurs years after a patient has been taking the drug, so it wouldn't show up during the clinical trial phase. So you provide that information to us.

Drug/drug interactions, drug/food interactions, now we have a more realistic view of what happens to this drug in a real person. And then increased severity or reporting frequency of known reactions. So maybe during the clinical trials, we were alerted to all of these side effects, but now, postmarketing, we know the

severity of these side effects and what the true frequency is.

Who should report? And the answer -- and many people have said it today -- is everyone and anyone who can: patients, healthcare providers, industry, advocates. Anyone who is aware of it, please do report to us.

This may be a little cheesy, but one person can make a difference. So let me share a story of Zach who works at DDI, and he was actually Hank's preceptor, right? Yes.

So two days before Christmas, Zach received a call from a physician in Louisiana in an anti-aging clinic who does chin liposuction. He had administered Wallcur saline solution to two patients. And like Val Jensen had said earlier, saline solution is salt water, normal saline. Everyone who goes into a hospital gets normal saline. So they got Wallcur saline solution.

We took note of it, submitted it to MedWatch and started investigating. But what we found out is Wallcur does not make normal saline solution.

Wallcur makes practice products, simulated solution.

So what happens if you take a practice, simulated solution and you inject it into people? Why is that a problem? It's not sterile. Right. So one patient was admitted to the hospital with sepsis and another patient got ill but was discharged.

This one report put us to action right away And within two days, we heard from CDC as well, that they had heard from the New York State Department, where there was an urgent care facility, administered Wallcur saline solution, and those patients got sick, very sick as well. So it does just take that one report to trigger FDA action.

So what should you report? Any event that is fatal, life-threatening, permanently disabling, requires or prolongs hospitalization, causes a birth defect, requires intervention, or there's a potential for harm.

Whether it's an adverse reaction or, like

Brian mentioned, a product quality problem, we want to know about it. Trust your judgment. If you think it's important enough that it matters, then just let us know.

A couple months ago, we had another example of an EpiPen, where someone injected the EpiPen and had a very bad bacterial infection, and we investigated. Luckily, that lot of EpiPen was fine and there were no problems. And it must have been either administration error or some sort of other contamination, but we would rather know about it and check it out before there's any harm to patients.

So how do you report? You can either report online or you can download our forms and mail it in. And again, if you think it is serious, call us. This is the MedWatch number right here. Call us and let us know so we can escalate it and take immediate action.

I'll go quickly over our three types of MedWatch forms. The first one is our mandatory form, 3500A, and this is used by industry. So

industry is required to report adverse reactions to us, so we wouldn't use this one.

Are healthcare professionals required to report adverse reactions to the FDA? True or false?

Yes. Good job, John. Yes. They learned. Yes, healthcare professionals can submit adverse reaction to the FDA through MedWatch 3500A, and this is a voluntary form, so they are not required to. And we understand the healthcare professionals are very busy, so if there's nothing else that you or they can report, please at least include these four components: the patient identifier, the event or problem, the reporter and the product. Without these four components, we cannot accept that report and include it in our data.

We understand, again, the quality of the report is very voluntary, too. We get some reports with just one single line, and we're thankful for that. And then we get some reports, which are a packet and includes the patient's medical history, the patient's labs, and a whole narrative on what

happened.

So whatever it is, we are grateful for it. Just please do report, please do submit.

The third form that we have is the MedWatch form 3500B. And OCHA, Heidi Marchand's group, Heidi was here earlier, they worked very hard on this form. They had a lot of listening sessions with consumers, with advocates, in order to create this form for consumers.

It contains the same four primary components as the healthcare professional form, but it's at a reading level, which is very easy to understand, so the general public can find it much easier to report.

You can also report online if you want to save trees and stamps. Go to our fda.gov/MedWatch website. Click on report a problem, and then you can choose two pathways in which to report.

If you want to report as a healthcare professional, you can go that way, and it will just ask you question after question to help you fill out the 3500 form, or you can click the consumer

patient button, and then that will ask you questions as well, and that will help you fill out the 3500B form.

What do we do with these reports? And we've heard about it today. Brian touched about it, too, so I'll go over this very quickly. But your reports go into our database -- it's called the FAERS database -- and then our evaluators will look at it.

I love the Discovery video, where the evaluators are looking like this. It made me think about some of the evaluators I know. They're very smart. But they do a very careful job of comparing your report with other reports within FDA, with other reports from other agencies, and with scientific literature, to really decide, is this an adverse reaction that's caused by this drug?

Sometimes we get someone calling into MedWatch or DDI. They have an adverse reaction. We tell them to submit a MedWatch form. They do. Two weeks later, they call back furious, you know, "Why have you not pulled this drug from the

market?"

You know, it takes time. It takes time. We want to be sure. We want to make sure that there is a direct correlation. So the postmarketing process is very, very intense, very thorough, and it can take months to years for us to complete this process. But at the end, if we do decide that there is a correlation with a drug and an adverse event, we will take regulatory action.

These are just some of the things that we can do. We can change the labeling to include adverse reaction section updates or warnings and precaution updates, add a black box warning. If we feel that we need more information, we can have postmarketing requirements or postmarketing commitments.

If we feel it needs even more restrictions, we can add on a risk evaluation and mitigation strategy, which was part of the Jeopardy. And in extreme cases, we can even pull the drug from the market in a market withdrawal.

Whenever we do something like this, we send

out a communication and the red bubble here, we send out a Dear Healthcare Provider letter or a drug safety communication. A drug safety communication is a very nice tool. It summarizes everything that is going on in this action. It includes the safety announcement. It includes separate information for the prescriber or the physician, and a separate information for the consumer, what to look out for, what they should do, and then a very nice data summary of all the things that FDA found and the reason why we are taking this action.

So you submit adverse reactions in. We evaluate it. We make a decision, take regulatory action, and then we need to communicate it back out to you so that you can take care of your patients and those that are using these medicines.

Like I mentioned before, the drug safety communication is especially good to communicate those slow moving actions. But back to our Wallcur situation. If we need to get information out quickly, we can use our CDER statements, we can

issue press releases, work with the company to issue a press release, and that's what we did.

So exactly one week, seven days after Zach got that first call, FDA put out something on our website saying watch out. Our CDER statement said, "FDA warns healthcare professionals not to inject patients with IV solutions from Wallcur of San Diego."

We didn't have a lot of information. We really didn't, but we needed to let people know right away. So we let them know it's for training purposes, that it's causing adverse reactions. And if you administer this to a patient, or if you were administered this Wallcur solution, please report it to MedWatch.

By two weeks later, we had 40 reports of patients who had been administered this Wallcur solution. By then, we realized that Wallcur solution was shipped to multiple hospitals and clinics. There were patients experiencing fever, chills, tremors, and headaches. Multiple patients hospitalized and one death, and that was all within

two weeks.

We also communicated that FDA was working with CDC to take these solutions and sample them to see if they were contaminated. We worked with a company to issue this recall. The company themselves, they changed the labeling of the package to make a very visible warning saying, "Do not administer this to patients."

We looked at the supply chain to find out how did this happen, how did this get into the supply chain? How did it go through pharmacy and nursing and actually get to the patients?

Val Jensen mentioned earlier this morning, one of the issues at that point is we were having a very severe normal saline shortage, so hospitals were thrilled to get these supplies of normal saline coming in, that no one even expected that they were practice solutions.

So we worked with drug shortages to better communicate with these hospitals; get your sources from here. We worked with the drug companies to rev up their manufacturing. We allowed importation

to come in. And these were just all different ways in which we worked together to resolve this problem.

Then four months later, when we finally closed the case, at that time, we did find out that these solutions had a lot of endotoxin and significant bacteria in them. So once it was injected into the patients, of course, it caused these infections.

You can't blame Wallcur. They never expected that this would be used in patients, but in the end there were 40 administrations of Wallcur solution; 26 patients with adverse reactions, 11 hospitalizations, and 2 deaths, and it happened very quickly.

So we're so thankful for that one doctor who called this in, that one report which triggered everything. If he hadn't done it, it could have gone on for months and caused even greater harm.

The takeaways, one report does make a difference. So if you feel it, if it just doesn't feel right, just let us know, and we'll take a look

at it.

We like to believe that you come to our website every day, but we've heard that's not the case. So we do what we can to send this information out to you. Each time we posted something to our website, we sent it out via our listserv, through Twitter and social media. And for drug safety communications, we'll do podcasts as well.

If you are not following us or are not subscribed to us, please do so, so that you can have the latest drug safety information.

We talked about MedWatch, and now finally, I want to talk about how you can engage with CDER. We've again had many touch points today, and I want to invite you to communicate with the Division of Drug Information as well.

Rich Moscicki mentioned earlier today how you can write in to the FDA, and many of you have done that. These are some of our writing campaigns just from 2015. Every time that you write in to the FDA, we will respond. You will recognize that

it has been cleared by multiple levels. And like Rich said this morning, there are many things that we cannot say because it's about an unapproved product. But we will give you all the information we can, and we will respond.

You, as advocates, you are doing great things. You are raising awareness on specific diseases. You are raising funding for research. You are attending high level meetings. You're playing Jeopardy at the FDA. I mean, this is visible stuff.

But then there's also parents and family members and friends, and they want to help their loved ones who have the disease as well. So for some of them, if they can just write in to the FDA, they've made an impact. They feel they've helped their family member. They feel like they are a part of this fight. So we do invite family members, advocates, to write in to us here in the Division of Drug Information, and we will do all that we can to respond back as well.

Today, we've heard about MedWatch. It's

very important for you to let us know if you sense that there is anything wrong with any product. We will review it, we will evaluate it, and we will send it back to you through our listserv, our emails, our website, our social media tools.

Finally, yes, talk to us. Here in the Division of Drug Information, many of us are parents, so we read these letters from you and your patients, and we cry. Many of us are children of parents who have Parkinson's. Some of us are caretakers of our parents. So, you know, we care.

There may be some things that we cannot do to get a drug approved, but if we can just listen, if we can just stand alongside you in this fight, we're very happy to do that. So thank you.

(Applause.)

DR. WHYTE: Thank you for that presentation. We do have time for a few questions. And while people are thinking of questions, I agree with Cat. It's great to see that we have 200,000 plus followers on Twitter. I only have 5,000. But when Dr. Oz has 3 million and the FDA only has 200,000,

we have some progress to make.

So are there any questions or any questions online?

(No response.)

DR. WHYTE: All right. Well, as Captain Chew said, we want to hear from folks. We want people to tell us about their concerns, and we have various mechanisms and strategies to do that. So thank you, Captain Chew, for that presentation.

(Applause.)

DR. WHYTE: Now, another true/false question before we hear about OTCs, or over the counter. So get your clickers ready, true or false. Drugs are sold over the counter, because the FDA has determined that they are safer than prescription drugs. True or false? I wish I had my Jeopardy music again, but I don't.

(Audience polled.)

DR. WHYTE: All right. And the correct answer is false. So good, that's 79 percent.

Now, we're going to hear about the ABC's of OTC's, and I'm delighted that Dr. Karen Mahoney is

available to speak with us this afternoon. She's the deputy director of the Division of Nonprescription Drug Products here at CDER. She's an endocrinologist by training and previously served as a diabetes team lead in the Division of Metabolic and Endocrine Drug Products.

Prior to joining FDA, she worked in academia as well as private medicine. She received an army scholarship for medical school. That's her fun fact, and was privileged to serve in the Army Medical Corps, including being chief of endocrine service at the Eisenhower Army Medical Center.

Please join me in welcoming Dr. Karen Mahoney.

(Applause.)

Presentation – Karen Mahoney

DR. MAHONEY: Hello. Good afternoon. It's lovely to be here. As John Whyte mentioned, I'm Karen Mahoney, and I'm the deputy director of the Division of Nonprescription Drugs here in the Center for Drugs. And as you can see, the title of my talk is the ABC's of OTC's, Little Known Facts

about OTC Drugs. And that title was actually given to me, but I actually really like it, because I do find that there a lot of things about OTC drugs that people don't know.

Throughout my talk, I'm going to have a few of these, quote, "little known facts." You can see that after it, I put a question mark because I actually think that you guys are quite a sophisticated audience, so you may very well know a lot of these things.

But my first little known fact is that there are over 100,000 marketed over-the-counter drug products, 100,000. And that's, of course, an enormous number, and it dwarfs many other categories of drugs.

In my division, my division director and I split the therapeutic areas. So I'm the signatory who's responsible for about half of these 100,000 drugs, and my boss is responsible for about half of them. And we have a terrific team who do great work to ensure the safety and efficacy of these OTC drugs. But we are a lean and mean machine,

considering that we have to manage 100,000 drugs.

Another little known fact, OTC drugs save billions of dollars in healthcare costs every year. And I'm not just talking about one or two billion. The last information that we have was $102 billion dollars in healthcare savings in the last care that was evaluated.

The reason they save money is, in large part, because when a consumer can self-diagnose and self-treat a minor ailment, and they don't go to the doctor or they don't go to the emergency room, that's a big cost savings. And the other reason that OTC drugs can save money is because they tend to cost less than prescription drugs. So they do save a ton of money every year.

A couple of other facts, on average, Americans make almost 3 billion trips a year to retail establishments to buy over-the-counter drugs. And the average consumer makes about 26 individual trips to buy OTC drugs every year, compared to about three trips to the doctor. So you can see that consumers choose OTC drugs much

more often than they choose to seek healthcare for their minor ailments. And I'll bet that all of you have at least one OTC drug in your medicine cabinet at home.

Another little known fact, there was a bill that created the OTC drug class as we know it, and that bill was sponsored by two senators who were also pharmacists. You can shout out if you want to, if anybody thinks they know one of their names.

AUDIENCE MEMBER: Durham-Humphrey

DR. MAHONEY: There you go. So I'll show you the next slide, and you'll be able to hear what they said. Durham and Humphrey.

Hubert Humphrey was vice president under President Johnson, and before that, he served as a senator for Minnesota. He was a pharmacist by training, and he had a big interest in drugs and drug safety. The co-sponsor of the amendment was Carl Durham, who represented North Carolina. He was also a pharmacist.

We're talking now about the Durham-Humphrey Amendment. Before 1951, prescription and

nonprescription drugs didn't really exist as two separate classes, so doctors essentially prescribed all drugs. But when this amendment passed, it established two drug classes.

It established what was called Rx Legend, which is prescription drugs, and those are drugs that require a practitioner's supervision, because of what was called the drug's toxicity, or "the potentiality for harmful effect," or the method of use. And the labeling of prescription drugs must indicate that it is by prescription only.

So what's an OTC drug? It's anything that's not a prescription drug. So that's interesting to me.

Another little known fact, technically, all drugs are OTC unless they're specifically determined to be prescription, not the other way around. As I mentioned earlier, a drug is prescription if it requires a healthcare practitioner for one reason or another. But that's not the default. The default is OTC.

Now, in reality, most of the low-hanging

fruit for OTC drugs, the easy ones have been developed. So most drug applications that we get now come in as prescription because they do require a healthcare practitioner, but that's not the default.

A little bit about the general characteristics of OTC drugs. OTC drugs do need to be safe. But you just heard that they don't have to be safer than prescription drugs, but they have to have an acceptable safety margin.

By that I mean this. All drugs have risks, but you balance the benefits and the risks. And we like for OTC drugs to have a wide safety margin, meaning that the likelihood of them being safe when used as directed is high.

They also have to be effective. They have to meet an effectiveness standard just the way that prescription drugs do. They have to have a low potential for abuse and for misuse. As we've emphasized before, a nonprescription drug, an OTC drug, cannot require a healthcare professional for safe and appropriate use.

They have to be labeled adequately. Consumers have to be able to self-diagnose. They have to be able to tell that they have the condition that the drug is intended to treat.

The labeling has to help you self-select. And by that I mean not only to know that you have the condition, but also to know that you don't have a reason why you shouldn't take the drug.

It also has to tell you how to self-administer. It has to have directions on it that people can understand so that they can use the drug correctly. And you also need to know when to stop using it. Many OTC drugs are self-limited in their labeling. They tell you don't take it for more than 10 days, don't take it for more than 2 weeks. They have to tell you how long you're supposed to take it.

Another little known fact, for some products, you might be surprised to learn that they're considered drugs. Here are some examples. A lot of times, people don't think of these things as drugs. Sunscreens are drugs. Antiseptic hand

rubs are drugs. Toothpastes, in large part, are drugs.

So what's a drug? The definition of a drug is more complicated than this, but the basic definition is that it's a substance that's intended for the diagnosis, cure, mitigation, treatment, or prevention of a disease.

So let's look at those types of products again. Sunscreens are intended for the prevention of sunburn, and people use them with the intention of hopefully reducing their likelihood of developing skin cancers; that's prevention.

Antiseptics are used to reduce bacteria on the skin, and people use them in the hope of reducing their chances of infection. And toothpaste is used to reduce the likelihood of developing caries, cavities, or gum disease.

Another little known fact, everything a consumer needs to know about how to use an OTC drug safely and effectively, and without any help from a healthcare provider, has to fit into a pretty small space.

So you guys have probably all seen this. This is called a drug facts label, and it's on every over-the-counter product. And it has to tell you, as I mentioned, everything you need to know, and you have to be able to do it all without talking to a healthcare professional.

It has to tell you all those things we talked about before, so that can make the decision about whether or not you have the disease. Is there something on here that tells you that you shouldn't take it? What are the directions how to use it safely and effectively, and when do you stop using it? All that has to fit into very little real estate, and some places, sometimes it's really little real estate.

Now, let's contrast that to the labeling for a prescription drug. The labeling for a prescription drug is called full prescribing information, and here's an example. You can see that this is many pages. It has graphs. It has a lot of text. It has charts.

This has a tremendous amount of information

in it, and it's intended for a doctor, a healthcare professional, so that they can guide a patient in how to use the drug correctly. And this isn't even a long full prescribing information. It's common for them to be 30 pages or more.

So you can see that if you have a prescription drug and you think you want to bring it over the counter, it's a huge challenge to distill the information in there, into what is really important, and it's everything a consumer needs to know and put it in this much space.

So another little known fact, I think you probably heard this morning about how prescription drugs are regulated. Generally, they are regulated in one way. But over-the-counter drugs are regulated in two different ways, and one of the ways they are regulated surprises a lot of people.

So we're talking about two pathways: the new drug application or the monograph. First, we'll talk about the one that's not so surprising.

The new drug application system is also the system that's used for the approval of prescription

drugs, and in that system, sponsors gather all the information, do studies, and put together a package, submit that application to us. We evaluate it and determine if it seems like the drug is safe and effective for use in the over-the-counter setting. And if it is, the drug is approved.

The sponsor has to come in with an application and get it approved before they can market it. And there's kind of three basic ways that it happens.

There are two kinds of what we call Rx-to-OTC switches, prescription to nonprescription. One of them is a full switch, and in that you have a drug that's being marketed prescription and the sponsor wants to switch it to over the counter, and they want to switch all uses of it from prescription to over the counter. So it's only available over the counter now; not available by prescription.

Then there's something called a partial switch, where the sponsor wants to switch some uses

of the drug, some indications of the drug, to over the counter, but they want to keep some indications prescription. Then less commonly, but it does occur, there are some drugs which are developed specifically for over-the-counter use, and the application is sent in for direct OTC approval.

I want to talk a little bit about some of the examples of partial Rx-to-OTC switches, which we talked about, and here's the tricky thing. You can't market the same OTC drug simultaneously for the exact same thing. You can only market it simultaneously OTC and prescription if there is a prescription use; that is a use that requires a learned intermediary.

So we've put some examples up here of the OTC uses of some types of drugs and what's still prescription. Topical antifungals, they're OTC for things like ringworm and athlete's foot. But they're still a prescription indication for a condition called tinea versicolor.

The proton pump inhibitors, these are things that you've heard of like Prilosec and Nexium.

Over the counter, they're used for the treatment of heartburn, but they're still prescription for the treatment of ulcers and for the treatment of erosive esophagitis. And you can see how those conditions -- they sound like things that need a doctor in order to manage them properly, so those are still Rx indications.

We also have the second-generation antihistamines. You've heard of things like Claritin. And that, over the counter, is for hay fever or other upper respiratory allergies. But on the Rx side, they're still used to treat chronic idiopathic urticaria, which is a kind of a chronic hives syndrome. And similarly, Flonase over the counter for hay fever, other upper respiratory allergies, but remains Rx for non-allergic rhinitis.

So here's some examples of things that underwent full switch. They were prescription before, now they're no longer prescription at all, they're only OTC. One of them you may have heard of is MiraLAX. It's used for the treatment of

constipation. Rhinocort and Nasacort also full OTC switches. They're used again for upper respiratory allergies.

Here's an example of something that went direct to OTC. Products that contain this were never Rx. Ecamsule is an ingredient that's contained in sunscreen, and it reduces UVA exposure.

You've heard of the UVA and UVB rays, and a lot of sunscreens protect against UVAs, but not many of them protect against UVA [sic]. Well, Ecamsule does. Their sponsor elected to come in under the NDA route and went direct to OTC. It was never prescription.

Another little known fact, there are special consumer studies that are sometimes done for OTC drugs, but they're not generally done for prescription drugs. So why is that?

Well, just as with prescription drugs, when a sponsor want to come in OTC, they still have to show that the drug is safe and effective for what they want to use if for. But, I'm getting back to

that drug facts label, they have to be able to understand how to do everything right just using that drug facts label.

So we use consumer studies to see if they get it, and if they can get it without a healthcare provider. And here's some types of consumer behavior studies.

Label comprehension studies, just as they sound, you give consumer behavior subjects the label. You determine whether or not if he can understand it. Professional social science researchers do this kind of work.

Self-selection studies. They're sort of like the next thing beyond label comprehension. Not only does the consumer have to understand the label, they also have to make a purchase decision. So from those we find out if consumers correctly determine that they have the condition, but also we want to know that they don't buy it when they shouldn't.

Another kind of study that is done sometimes on the prescription side also, but also on the OTC

side, are human factor studies. These are mostly done when you have a device involved, and they're really like evaluating the physical interaction between the consumer and the device. Can they physically use it correctly to administer whatever medicine is supposed to administer?

Then finally, actual use studies. Not all over-the-counter drugs require an actual use study for approval, but it's a more comprehensive kind of study. It's sort of soup to nuts. It includes everything from the consumer selecting to purchase the drug, through them using it as they're supposed to, and they all have the condition that the drug is supposed to treat.

Data are collected that tell us whether they're using it correctly. If not, how are they misusing and why are they misusing it? And that gives us a lot of information that helps us to know whether it's likely that if the drug were to be approved OTC, if consumers, millions of consumers sometimes, would be able to use it correctly.

So on to the sort of surprising method of

OTC regulation. It's formally called the OTC Drug Review, but most people refer to it as the monograph. Back in 1962, a law was passed that required drugs to demonstrate that they were effective before they could be approved and go on the market. And that law essentially resulted in the new drug application system.

But at that time, we had a big problem. We already had over 100,000 over-the-counter drug products on the market. So what do you do with those? You can't suddenly say that all those drugs are misbranded, so you've just got to take them off the market. People need those drugs, and there's huge economic impact of that. And also, the FDA couldn't possibly review 100,000 NDAs.

So the solution they came up with was in 1972, they set up the monograph system. And what this was, was they set up expert panels, mostly outside experts, and they looked at over-the-counter drug ingredients, and they did it by therapeutic category.

So what's a therapeutic category? Things

like this. Here are a number of examples. I won't read them all. But for example, antacids are one; analgesics are one; dandruff products are one.

So for each of these therapeutic categories and others, a panel was set up and what did they do? Well, they developed a sort of a recipe book for what the marketing requirements would be for an over-the-counter drug. And what that is, they were trying to determine things like what active ingredients could be in a drug for this condition? What dosage forms could it be in? Tablets, suspensions? What should the labeling be? What should the amount of the dosage be?

What they were trying to develop was a list and an explanation of what are called GRASE, G-R-A-S-E, GRASE conditions, which mean generally recognized as safe and effective. So what they were trying to do was come up with a document that says, if you do everything this way, if you follow this recipe, the conditions under which you market that drug would generally be recognized as safe and effective.

Here's the interesting thing. If you follow everything in the recipe book, you can market your drug without coming to the FDA every time for every single product. As long as you follow all the rules, you can market it without prior approval of each product.

Now, the expert panels finished many of the monographs; not all of them. And final monographs are published in the Federal Register, so it's publicly available for sponsors to access and use to develop monograph drugs.

But here's a catch with the monograph system. It is cumbersome. It requires three-part rulemaking, and it's an entirely public process. So we first have to publish usually an advanced notice of proposed rulemaking in the Federal Register, and then there's a public comment period.

It comes back to us. We evaluate the comments. Then we write a tentative form of the monograph. We publish that. That again goes out for public comment. And then finally, it will come in, in final monograph form. But there are lots of

steps in there, and they include a number of steps outside the FDA.

For example, it often has to go all the way up to the White House Office of Management and Budget. And as you can imagine, all those steps can take a lot of time. So that creates quite a burdensome system.

Rulemaking takes time. And another issue is, back when they were thinking about developing the monograph, they thought, oh, let's create this recipe book and we're one and done. If we write that recipe, we're all done with that therapeutic category, right? Check.

But science moves on. Science develops. We learn new things about safety. So the monograph is a living document, and we're always needing to change it, and it's very hard to change it. And a colleague gave me these pictures on this slide as evidence that time does march on.

(Laughter.)

DR. MAHONEY: All right. We talked a little bit about the two OTC regulatory pathways, and

here's some differences. There's only a couple of them that I wanted to talk about since we've already covered most of them.

One of them, I kind of mentioned it, it's an entirely public process. All of the data that FDA uses to make its decision about whether or not to call all the conditions for that monograph GRASE, they have to be public. They're put into a public docket. Anybody can look at them and everything that we use to make our decision has to be out there and public.

On the other hand, NDAs, when a new drug application is filed, it's confidential at filing. And the information about what FDA used to make its decision about whether to approve it is generally not available until the drug is approved.

Another difference between the new drug application process and the monograph process is that the new drug application process has user fees. There's the Prescription Drug User Fee Act and others. And what those are, are the users of our services, which are drug companies when they

want to send in a drug application, the review of a drug costs a lot of money. There are many highly educated people who have to review it. We have infrastructure costs.

So there have been acts that have created user fee programs. And those are available for drugs that are under new drug applications, but there are no user fees for monograph drugs.

As you can imagine, it's hard to do what we need to do for 100,000 drugs. Not all of them are monograph, but most of the drugs, most of OTC drugs out there are monograph drugs. It's hard to do it with very limited resources.

I've just told you what the differences are between an NDA and a monograph, so we're going to have a little fun here. So on one side of the slide you have NDA drugs and on one side you have monographs, and I'm going to ask you to raise your hand about which side is monograph.

So first of all, and I'm talking about your left, how many people think the drugs on the left are monograph products?

(Show of hands.)

DR. MAHONEY: And how many people think the drugs on the right are monograph products?

(Show of hands.)

DR. MAHONEY: You guys are good. You guys are good. That's right.

You kind of tell, because, remember, monograph is often old drugs and NDA a lot of newer drugs. So you can see those newer names up there like Pepcid and Claritin. So you're absolutely right. Got that.

So you guys are awesome. I guess my job is done, but it's not quite done. I have three more slides.

Another little known fact, the Federal Trade Commission, not the FDA, regulates OTC drug advertising. The FDA does regulate prescription drug advertising. And that's a little bit surprising to a lot of people. A lot of people think the FDA would be the one who would evaluate nonprescription drug promotion, but we don't. The Federal Trade Commission has authority over that.

So what do I think about the future of OTC drugs? Well I definitely think that we're going to have more prescription drugs that want to come over the counter. And I think that some of these will be in therapeutic areas for which we don't currently have over-the-counter options. That's one thing that I really think will happen.

Another thing -- so you've already heard me whine about little the drug facts label is -- we're hoping that there will be a means to harvest technology to augment that drug facts label and perhaps to allow some drugs that otherwise couldn't come over the counter, to be over the counter. And for that, we are trying to develop a regulatory framework for something called the Nonprescription Safe Use Regulatory Expansion or NSURE.

What I'm talking about, the technology that I'm talking about, are things like apps or maybe smart devices, things like that, that could accompany the DFL and help consumers to be able to use a drug OTC that they might otherwise not have been able to.

You also heard earlier about how difficult the current monograph regulatory system is. We are hoping the future is going to bring reforms to that regulatory system to make it more streamlined, and to make it faster for us to complete monographs and to add safety information, and maybe even to be able to make other changes to the monograph to expand what it can be used for.

I'm going to give you some contact information here. In general, inquiries about over-the-counter drugs go to the Division of Drug Information, and that's the contact information there. Also, you've already heard about MedWatch, and I've given you the link to the MedWatch page.

I'd like to thank you very much for your attention. And I don't know if there's time for questions, but if there are, I'm happy to answer some.

DR. WHYTE: Thank you, Dr. Mahoney.

We do have a question that came in online, and folks can line up if they have some questions at the mics. One of the questions online was, "Why

does the drug facts label appear on the back of the product rather than the front?"

DR. MAHONEY: I have to tell you, we have an associate director for labeling, so I'm not 100 percent the expert in all of the little details of the regulations surrounding it. But the drug facts label actually is not always on the back. It's sometimes on other areas.

But in general, it does not have to be on the front of the package. The front of the package is usually what we call the principal display panel, and it has certain required elements on it. It has to have the common name of the drug on it. It has to have the strength of it. There are certain things that have to be on the principal display panel.

You may notice sometimes that parts of the drug facts label are actually on the side of the package. But each time an NDA product comes in, we are able to evaluate the packaging that they're proposing, and we're able to do what we can to be sure that that drug facts label is readable and

accessible.

Monograph drugs are also held to the same standards under the regulations, but as I mentioned earlier, they don't come in for pre-approval before they're marketed.

MR. WEINBERG: Hi. Some of the over-the-counter drugs on the market have little evidence or no evidence of efficacy. There's no evidence for any homeopathic products working, for example, and some of the cold medicines, also there's equivocal evidence or no evidence.

DR. MAHONEY: I'm sorry. Can you say it a little bit louder? I heard the part about homeopathic, but what did you say next?

MR. WEINBERG: What are you doing to take drugs off the market that don't have an evidence base for effectiveness, including homeopathic drugs and some cold medicines, which have very little evidence for their efficacy?

DR. MAHONEY: Okay. So at this point, we haven't been granted authority over homeopathic drugs. I hear what you're saying, and I know that

that's a big concern. But at this point, we don't have authority over homeopathic drugs.

However, when we receive information that suggests that a marketed over-the-counter drug product -- not a homeopathic product, but a drug product -- might not be effective, we do address that. And there have been examples where we have received a study that suggested that it might not be effective, and we've pursued it. And it is possible for us to remove an indication for an OTC drug product.

DR. WHYTE: A question from online?

DR. HOANG: I have another one. "For partial over-the-counter drugs, how do you prevent patients from buying it over the counter and using it for prescription purposes?"

DR. MAHONEY: We can't, and that's the simple answer. But that's a big concern. We do ensure that the labeling makes it clear that there is a limited duration of use for many of these, but we don't have any ability to force consumers to not buy more of it or use it for longer than they

should.

One thing that is a challenge for us now is what we call the Costco effect. Places like Costco and other -- not to name one name, but many discount retailers, they want very large package sizes of things, and that's a challenge for us. We are concerned about that issue.

We do have the ability, to some extent, to say how many drugs can be in a package, but it's somewhat limited. But that's an area of interest to us, and we're trying to determine whether there are ways that we can sort of address that.

But you're absolutely right. We can say that a bottle of a drug can only have 14 pills in it, but there's nothing to prevent someone from buying a hundred bottles and using it all year.

DR. WHYTE: Okay. Thank you.

(Applause.)

DR. WHYTE: Okay. So we're in the home stretch. We're going to take a 15 minute break. And when we come back, we're going to hear from two advocacy groups that are going to talk about what

they define as successful and effective engagement with the FDA, and then I'm going to give you some final words of wisdom and some tips on how to be an effective advocate.

But before we break, we always wait until the end to thank folks, and I want to take a minute while folks are still here. I want to recognize certain members of my team, especially Laurie Haughey, at the front of the room. If Laurie can stand up.

(Applause.)

DR. WHYTE: Laurie really has done an enormous amount of work helping to plan it, coming up with titles. So it deserves an enormous amount of credit. It was her idea for Jeopardy and the quiz questions, which I think has gone over very well.

I also wanted to recognize Rea Blakey on my staff, who many of you may recognize from working at ABC News for a long time and CNN, really who has helped pull this day together.

(Applause.)

DR. WHYTE: Along with Dave Boggs. Dave is a health communication specialist and is filling in as one of our computer IT folks. So we wear lots of different hats in my group. And Hank Hoang, who gave an excellent presentation this morning, who actually worked to coordinate everyone else's presentations.

(Applause.)

DR. WHYTE: Junyang Wang's not a photographer by trade, but is filling in today. And for those folks like Brian who didn't like his picture, well they should have sent us one; otherwise we find them.

(Laughter.)

DR. WHYTE: I want to thank Shawn Brooks and Chris Melton who also helped develop the agenda for this week, as well as Sadhna Khatri. It really has been a huge team effort at the staff level, so I want to thank them.

With that, we'll take a 15 minute break. And as I said, we're in the home stretch, and we will end promptly. Thank you.

(Applause.)

(Whereupon, at 2:45 p.m., a recess was taken.)

DR. WHYTE: We're going to go ahead and get started. If Cynthia Bens and Bernadette O'Donoghue can come up to the podium.

Okay. So you've been hearing from FDA officials for the last six hours or so, so now is an opportunity to hear from some other folks.

I want to preface by we haven't told anybody what to say, so hopefully they won't embarrass me. But they're going to talk about what is successful patient engagement with the Food & Drug Administration.

First, we're going to hear from Cynthia Bens, who's the vice president of public policy at the Alliance for Aging Research. In this capacity, Cynthia's responsible for guiding the organization's federal policy work, representing the alliance in multiple coalitions.

For the past 14 years, she's worked to inform federal policy makers and educate the public

on a variety of issues, particularly in the development of interventions to treat and prevent many debilitating age-related disease, to improve access and decrease barriers to needed treatments and therapies, and to improve the coordination and quality of care that seniors receive.

We're also going to hear from Bernadette O'Donoghue, who's the executive director at the Leukemia & Lymphoma Society. Bernadette provides strategic leadership in management of LLS public policy agenda and regulatory affairs initiatives. She has coordinated and developed the society's strategic policy positions that encourage sustainable access for blood cancer patients to quality affordable care and coordinated healthcare.

I've had the opportunity to work with both of these women over the past year, so I am eager to hear what they say. First, we'll hear from Cynthia; then we'll hear from Bernadette, and we should have some back and forth. And then the audience will have time to ask them questions as to how they've been successful and what success means.

So thank both of you for taking time to be here today.

Presentation – Cynthia Bens

MS. BENS: I'd first like to thank the FDA for the opportunity to be here. I think this is a really important meeting and something that's a long time coming. We're really humbled as an organization to be recognized as a pro in interacting with CDER.

I'd say that just looking around the room, there are a number of you here today who could give an equally effective talk on this issue, and I will do my best to try to capture some of the major themes that I think a lot of you would also say.

But I can only also say that our successes come through persistence and effective mimicking of a lot of the plays that have come from the playbook of other diseases that you heard about a bit about this morning.

First, I'm just going to start by telling you a little bit about our organization, the Alliance for Aging Research. We were started

30 years ago, and we were started because there were a number of different aging organizations already in existence that were focusing on services and supports for the elderly, and also really involved in policy issues related to preserving programs like Social Security and Medicare.

But there was no equivalent of the American Cancer Society or the American Heart Association for aging. Nobody was actually looking at aging and the potential of aging research, and the application of that research to help keep people healthier longer.

So we really have our roots in advocating for federal funding of aging research through the National Institutes of Health. It was about 10 years ago that we started looking at the diseases that disproportionately impact older adults and their families, the healthcare system, and sort of cross walked that list with the prospects for drug development and having effective therapies for ameliorating them.

The first disease that really came front and

center to us was Alzheimer's disease. Alzheimer's disease, I think we all know, has a tremendous human and economic burden, but it also was conspicuously -- there was a real gap to fill in having one single point of advocacy for groups that wanted to engage with the Food & Drug Administration on issues related to drug development for Alzheimer's disease.

So we started the Accelerate Cures and Treatments for Alzheimer's Disease Coalition or ACT-AD for short. We now have more than 50 non-profit member organizations. We also work with a number of the pharmaceutical companies who are developing both symptomatic and disease modifying, we hope, therapeutics in this space.

We have a science advisory board, and our science advisory board is made up of individuals who both understand the disease pathology to the extent we know it, as well as people who have been involved in some of the large scale trials that have been funded by the National Institutes of Health. And we have a former head of the neurology

review division at FDA also on our science advisory board.

Really, what we're doing is we're trying to serve as that single point of advocacy for clearing the pathway, so when there an effective therapy for Alzheimer's disease, that FDA is poised to approve that drug and has the best knowledge at their disposal.

But when we came to the table, there were a number of things that we thought should be also in play at FDA. We were surprised that there was no patient representative program for Alzheimer's disease. I think you heard a bit about that from Heidi Marchand this morning and how important having one of those programs is for making sure that patients and caregiver voices are represented, particularly at the point of advisory committee meetings. So we asked FDA to establish one, and they did.

We also helped to serve a role linking them with some of our member organizations to get patients and caregivers qualified to sit on an

advisory committee if a drug is successful at getting at that point.

We also wanted an Office of Alzheimer's at FDA. That does not exist, so obviously we were not successful in that. But FDA did the next best thing and set up what is known as the Neurology Across FDA Working Group. And it's unique in that it was a mechanism for the different centers and offices at FDA to come together to discuss cross-cutting issues internally, pool and share expertise, and that's something that I think a number of diseases are looking to do moving forward. But that was something that they did voluntarily after we asked them to do that, without much pressure, so that was great.

They also agreed to work with us on an annual meeting. This is outside of any IND process and not product specific, but we wanted it to be different. A lot of these conversations typically happen between companies and FDA, or they happen between specific communities, and we thought it was important for everybody to be at the table.

So at our meetings we have patients, caregivers, patient advocacy groups, industry, NIH and FDA. They all come to the table. And it's a pretty big effort. It takes us about a year to pull them together. But we come together around a single issue and we take on meaty issues.

We've had a number of different meetings talking about issues related to clinically meaningful benefit in Alzheimer's treatment. We've also looked at all of the disappointment that's happened in phase 2 trials for Alzheimer's disease and why they haven't been predictive of success in phase 3 and how we might be able to change that.

Based on a suggestion of FDA, we even took on issues related to combination therapy development. And prior to having those types of conversations in our meetings, companies weren't even thinking about combining multiple treatments for Alzheimer's disease. And just seeing a willingness by regulators in wanting to start that dialogue, there is interest now among the companies, so we're really pleased by that.

There was also some talk this morning about how patient advocacy groups might engage with FDA related to disease-specific guidance. When we started, there was no disease specific guidance related to Alzheimer's disease, and it was really frustrating to everyone.

But FDA, about I think it was two-and-a-half years ago now, they did issue a draft guidance on early Alzheimer's drug development. What that really meant, it wasn't a lot different than what they had been saying in different meetings about what they were thinking related to early Alzheimer's development, but it meant something to us, because it meant that they were really ready to put a line in the sand and say, this is what we think is a reasonable approach to drug development for early Alzheimer's disease now. If there is going to be a therapy that's going to successfully make it to an accelerated approval pathway, these are the types of things you need to consider.

So it was a really big win, and we don't think it would have happened without the just

constant pressure from the outside in hammering home that FDA really did need to do that.

I'm going to switch gears and talk about another effort that we are involved in. It's called the Aging in Motion Coalition, and this is a coalition that we formed in 2011, and it has to do with sarcopenia.

Sarcopenia is not a household name. I get it. Probably most of the room doesn't even know what it is, and I didn't before I started working at my organization. But if you have a frail older adult in your family or in your neighborhood and you see them walking slowly and having difficulty just getting in and out of cars, it's most likely related to their muscle wasting.

So sarcopenia is a clinical condition that's related to muscle wasting in the elderly. And in and of itself, it's a disease. It's been studied for about 20 years. It not only causes disability and complications on its own, but it is associated with challenges in recovering from hip fracture, puts people at higher risk for falls. And if

you're managing a comorbid condition that's related to age like COPD, it makes it that much more difficult to have improved outcomes.

So we knew that there were some pharmacologic treatments that were being tested. They were not successful. And we started to look at why that was. So we started this coalition just looking at the gaps, what was actually happening in these trials. They were intended to build muscle. You would think that building muscle was going to make people better. That wasn't the case.

So we pulled together mostly science advisory boards, because they had been the one that were studying it for 20 years, and also various companies, because this has a nutritional component, it has a physical activity component, it has a screening component. But there are drug treatments that people are testing for it. And we wanted to know what we could do to help move the needle on it.

The first thing we did was we, to our surprise, found out that sarcopenia did not have a

diagnosis code. So one of the things that we had to take on is actually getting it recognized as a disease that can be diagnosed. So we're doing that with the CDC and CMS, trying to establish that.

But with FDA, we're taking a totally different tack than Alzheimer's disease. There are no qualified endpoints for use in clinical trials for sarcopenia, despite the fact that there have been some embedded in some of the trials that haven't succeeded, but we think that there are validated measures out there.

So we are going through the qualification process to have two functional measures qualified as outcome measures for use in clinical trials. And if we're successful, these are going to be endpoints that are available to anyone for use who want initially in a subset of patients with sarcopenia who are, because of their muscle weakness, having challenges recovering from an already fractured hip. But it's our foot in the door.

Then the last thing, we thought because of

the growing burden of this disease in the older population, and it's a rapidly growing segment of the population, we wanted to encourage FDA to hold a patient focused drug development meeting on this because we know that there's a lot of people out there with it. And we think that the community would benefit from having that perspective, largely because there is going to be a patient reported outcome component if there is going to be a successful drug trial.

FDA has already sort of said they think that the PROs are very important to this specific disease, and we think that an FDA patient-focused, drug development meeting was really important at this time, and we were fortunate that they agreed.

So it's going to be the last, but we are happy that it's going to happen in FY2017 and are really looking forward to working with FDA on that.

So why am I telling you guys all this? I'm telling you about it because we had no one to tell us what to do. We were trying to figure all of this out. So I wanted to just take a moment just

let you hear about some of the lessons that we learned along the way that might be helpful to you, and let you know that we're here as a resource. We didn't, by any means, create this space. We figured a few things out along the way, but we want to see other people succeed in doing this.

The first thing I'd say is we're not special. Many of you know that I come from a large family from northeastern Pennsylvania, and my family takes every opportunity to remind me how normal and how unimpressive I am, especially my three older brothers.

So I am not special. I'm not a scientist. I'm not a regulatory expert, and neither are any of the colleagues I work with. We just put in the time. And I would say just put in the time to learning as much as you can about the clinical trial process and about drug development.

We did it because we just want to see human suffering in the older population, we want it gone. We want people aging the way that everyone wants to age, in their home, as vibrant as they can be.

So all of you can do this, and it's really going to help, the more that you learn about the process. Identify what type of information is actually useful for the regulatory process and also help you identify the gaps.

I mean, we were really good at filling gaps, and that's the best thing that I can say. The more that you learn about it, you'll see where the gaps are. And I think from the patient advocacy perspective, you bring a lot because you're almost sort of like a common sense dispenser in an area where people sort of get wrapped a lot into the science. So that's useful.

I would say work with every advocacy group in your disease space that you can. We run two coalitions, and we know that's not always easy, but it's really important. And I think as we're moving into this era of the patient-focused drug development effort being externally led, it's going to be even more critical if we want to bring the regulatory perspective to the table.

We're all sort of singing from the same

choir book, and we're addressing the needs of the patients that we know are out there. So I would say to the extent you can, work with other advocacy groups in your space and leverage their talents to the extent you can.

Also, reconcile your goals with that of industry and the research community. I know sometimes people don't understand that that's possible, but it is. And it's particularly a lot more easy to do that if there's not a specific product tied to it.

I think a lot of what I heard this morning, those of you who asked questions, are working in areas where you want to see more development, so that's not already there. So it's almost less of a concern for you and talking to industry is not a bad thing.

I would just put that out there, you'll learn a lot about a lot, just by talking about industry and the struggles they go through, through the drug development process.

I would say, listen to FDA when they speak.

FDA speaks to the community in a lot of indirect ways. It sounds simple, but sign up for every listserv that FDA has and read those super boring Federal Register table of contents, and everything related to FDA, because a lot of information comes out that way.

I'd give one example where we found really useful information just from being on the blog listserv that comes out of the director's office. FDA had put out a targeted drug development report, not specific to Alzheimer's disease, and Alzheimer's disease wasn't even one of the diseases that was focused on.

It was used as examples where there questions raised about the understanding of the pathology of disease and where there are gaps in biomarkers and challenges with reliability, and it went completely unnoticed by a lot of people in the Alzheimer's community.

But we found it, we read it, and we talked to the review division and said, do you think that these things that are ripe for conversation? So we

had our last annual meeting addressing those specific things, but it never would have happened unless somebody was just really paying attention to what FDA was saying.

I would just close this whole segment by saying temper your expectations. A lot of the times, I think that one of the reasons I'm here is because neither of the diseases we work in actually have really successful treatments up until this point as a result of our advocacy, but we have moved the needle.

I would just say that we're at a point where we think that our engagement in these two diseases has really gotten FDA to sit up and notice. And also, meet them as informed as they can be, so when there is an effective therapy, that they are poised to make what we hope is the right decision and approve them.

We've just been on this journey with FDA, and we think it's been really important and we've done our job as advocates. And it's hard. It's really hard to be patient.

I'd also say that one thing that's also been important to us is to acknowledge when FDA has gone above and beyond. I think Dr. Woodcock said this morning that it's sort of an output driven agency, and customer service sometimes is not what everyone here would like to see.

But many times they're only publicly acknowledged when they're involved in something controversial or it's been perceived that they've maybe not made the right call about something or they've fallen short. And I think it's important that when they've done something important in your disease, or even something really small in your disease, that you recognize it, and you recognize it publicly. And we do that a lot.

We really praised FDA for putting out the disease specific guidance. When they came out with patient-focused drug development meeting on sarcopenia, we were as surprised as anyone. It was all really because of them. We couldn't take a lot of credit except for putting maybe some persuasive comments together. So if you have the opportunity,

just praise the FDA.

I know John Whyte thanked a whole bunch of people who are here for the meeting, but I think everybody at FDA really deserves a big thank you for everything they do every day to keep us safe and promote our health.

We've gone a step further and come up, just for this meeting, with our CDER Hall of Fame for engagement, because engagement really is a two-way street. And we feel that these people really exemplify the spirit of being patient centered and patient focused, and they've been doing it for a long time, not just because it's a buzzword now.

In particular I'd like to recognize Billy Dunn, Eric Bastings, and Nick Kozauer from the Division of Neurology Products, and also Jean Marc Guettier from DMEP, and Elektra Papadopolous from the Clinical Outcomes Assessment Team.

If their bosses are here or watching, you should really use them as the model for effective patient engagement because they really do a great job at being responsive to us. And at the very

least, I think they deserve a gold star.

So I'll stop there. Thanks again, FDA, and be happy to answer any questions. Thanks.

(Applause.)

DR. WHYTE: I think we'll save questions for the end. I did not know I was going to win a Hall of Fame award, so thank you.

MS. BENS: I missed Jeopardy's.

DR. WHYTE: Well, okay. All right. I have a three-year-old son, and he's very interested in trophies. It'd be nice if you had a trophy that I could bring home.

MS. BENS: Well, we'll have to work on that.

(Laughter.)

DR. WHYTE: Okay. With that, we'll hear from Bernadette, and then we'll have time for questions.

Presentation – Bernadette O'Donoghue

MS. O'DONOGHUE: Thank you, John.

Thank you so much for inviting me. I'm representing the Leukemia Lymphoma Society today at this meeting. I'm very pleased to be here. And

I'm approaching it a little differently, even than Cynthia, and I think much of what she said, I will reiterate, but probably in a slightly different format. I thought what I would do is just essentially tell you how we do it at the LLS and how we started three years ago, and where we are today.

To put it in context, I have to tell you that, except for the last three years, I have worked with the biotech industry. And in the biotech industry, I learned a lot about the drug development process from the beginning to bedside, from the invention to the bedside.

I also was responsible for the European and U.S. markets for market access, and that would include everything on the commercial side of the business to include manage markets, contracting, pricing, anything with pharmacoeconomics; anything that actually supported the commercialization of a product.

So I was very schooled in the commercial side of the business and thought I knew a lot about

the FDA. But I have to tell you, after listening today to everything that was presented, I realize there was an awful lot I did not know. So I did learn a lot today, and I hope all of you did also. I'm also very aware that it's 3:30 in the afternoon. It's the end of a long day, and I'm probably going to be very succinct in my comments.

But three years ago, when I joined the Leukemia Lymphoma Society -- and we represent 1.2 million people who either live with an active blood cancer or are in remission for blood cancers. When I got to the organization, they were relatively new in the regulatory space. We had just opened the Washington, D.C. office.

For the most part, I would say that we focused on submitting comments to regulatory guidance or something in the Federal Register, and beyond that we did not do a whole lot. We also were aware that the term du jour was "patient engagement," specifically after PDUFA V, and what did that really mean?

Now, we are a patient advocacy group, and

what does that really mean? How do you define that? It's advocating for or supporting or recommending. But if we were to really represent patients in meaningful way, we needed to look at what we were doing in an entirely different way. So we thought that we probably should take a look at engaging with the patient more and what did that look like?

So the first question we asked ourselves was, what is successful advocacy? What does it look like? And I immediately went to where I was my entire career. Successful advocacy means you get a drug approved or a device approved.

Well LLS is not a research organization. They were not then; maybe we might be approaching things a little differently now. But then, we were not a research organization. We did not engage in primary research. We funded, we provided funding to researchers from our therapy acceleration program, but we were not a research organization.

So that required a shift in mindset, maybe even a shift in culture within LLS, and it required

a lot of education with regard to that. So I thought to myself, how am I going to get an organization -- this was my job -- to actually shift a mindset? And I thought, well, I just joined LLS three years ago, and how did I go about understanding the LLS and the culture? Well, I looked at the mission of LLS, and I said, "Well, I'll start there."

So I looked at the mission at the FDA, the CDER specifically, and three things stood out: safe and effective drugs; quality and the integrity of marketed products; and promoting the safe use of products. And I thought, "Well, it aligns with our mission in that we advocate for and we're supportive of the development and the approval of products that are safe and effective and that are quality." We also advocate for products, getting the right product to the right patient at the right time. So there's real alignment here, and we were very pleased about that.

The next question that we asked was, well, how am I going to then move to engaging even more?

And I thought, "Well, Dr. Woodcock, everybody knows who Dr. Woodcock is. Everybody knows who the commissioner is. I could get our CEO, Louis DeGennaro, to call Dr. Woodcock," not that it's that easy, but nonetheless.

I thought to myself, "Well, what did I do when I actually joined the LLS? How did I get to know the organization?" And I thought, "Well, what you have to do is you have to identify and establish relationships with everybody across the organization at all levels."

Don't just rely on Dr. Woodcock. She has highly educated, experienced teams of people whose job is to develop products, bring them to market, and make them available for patients. So I said, "I'll start there."

What I also realized is just as any relationship requires time and effort, it also requires collaboration, negotiation, and some give and take. So I thought, "I'll apply those very same principles with the FDA."

So we went ahead, and we started identifying

the right people with whom to interact to further our mission. And what I'd like to do is give you an example then in practical terms as to how that actually played out.

So remember, the term du jour is "patient engagement." So I thought, "FDA has committed to having 20 plus meetings. They're also very open about the fact that they want patient groups to actually convene their own externally-led meeting, because they don't have the resources or the time internally to do it."

So I was very fortunate to make the acquaintance of Dr. Whyte and his staff. So for the last year-and-a-half, I have been working with Dr. Whyte and his staff to identify the steps to take to actually convene our own -- and it's not a patient-focused drug development. It is a patient-focused, drug development type of meeting.

We also listened very carefully to what Dr. Mullin and Dr. Woodcock was saying about we knew to take the data and actually have data that is quantifiable, scientific, and reproducible. How

do we go about that?

So again, we were very cognizant of the fact that as a regulatory agency, there are limits within which any regulatory agency can work. As a potential reviewer of data, they cannot be around the table as a stakeholder, per se, when we are discussing the methodology and we're having discussions around how we would actually approach the project. But they are very open and available to actually review whatever decisions are made along the continuum of actually developing a patient-focused type of drug development meeting.

So we put together, again, under the guidance and with input from -- not so much guidance; let me withdraw that word -- with input from the FDA and Dr. Whyte and his team with regard to the steps to take if we wanted to convene such a meeting. We also listened very carefully to what the FDA was saying in terms of the best type of meetings to have are their opened convening meetings in areas where there is an unmet medical need.

Now, blood cancers, in general, the patients have been very, very lucky in the last couple of years in that the newer products that have been approved -- many of the new products that actually were approved in the last 24 months, have been in blood cancers. But there is a blood cancer called acute myeloid leukemia, which is an orphan drug disease, and there really hasn't been a new standard of care or a new product approved in this space for the last two or three decades. So there's a real unmet medical need there.

It actually is a complex and heterogeneous group of approximately 20 different types of blood cancers. There's more than 10,000 deaths in the United States every year from this AML with a very poor survival prognosis.

So what I would say to you is this. We started working on convening our own meeting at least 12 months ago, and that effort is culminating in us having our own LLS, FDA meeting, next Wednesday, April 6, with AML.

We could not have done it without the input

of the FDA. We could not have done it without the generosity of their time and attention to what we were trying to do. So if I was to summarize, and if was to make, not so much recommendations, but what our experience has been, it is to understand where your mission overlaps with the agency's mission.

Identify the appropriate people at all levels. They are ready, willing, and able to actually work with any patient group.

Be very aware that the agency has demands on their time and effort at all levels at all times, so make sure that you're talking about an area of unmet medical need. And we heard this, this morning, if indeed there is a need to request a meeting, an externally-led meeting, then collaborate with others who are in the same space as you are.

Make sure that you include a variety of stakeholders because if we're going to further the science of patient-focused drug development, we need to ensure that it's relevant for all

stakeholders. There's no sense in developing information that one stakeholder finds irrelevant. We're never going to further the science from that perspective.

We spoke with patients in the space. We have at least 25 to 30 hours of conversations with patients who actually have AML and they're survivors. So we learned as well from the real experience of patients and they're survivors. We actually spoke with researchers, clinicians in the field, and we also spoke with manufacturers to see what their perspective was.

So I thank the FDA for their support with our initiative. I think we are successful, and I'm very pleased with where we're at in terms of the efforts over the last 12 months. We could not have done it alone.

I would suggest that, as I say, you use the expertise within the agency. There's really no need to -- unless you're really not getting anywhere -- to escalate it maybe to somebody like Dr. Whyte. But also, don't be so quick to run to

Congress for solutions. I think the FDA is open to working with us, and I do thank them. I think our success is very much attributed to the collaboration we've had with the FDA.

So my thank you also for your time and attention today. Thank you.

(Applause.)

DR. WHYTE: Thank you both for your advice and suggestions. We have an opportunity for questions, for all of you to ask questions of Bernadette and Cynthia. So if you have any questions, feel free to come up.

You know, Bernadette, I've only been here two years, so I can't believe it's been a whole year working with -- half of my time has been working on our meeting next week, but that's how long it takes.

Any questions?

(No response.)

DR. WHYTE: I'll ask one question that both of you can respond to.

I've heard from folks, and I mentioned to

both of you, that some advocacy groups will say your job is to get the drug approved. And if you don't get the drug approved or you don't get the disease on the list of diseases to be discussed at PFDD, you're not successful. And that's what you're here to do.

So could you address that a little? Is it lack of success if you don't get the drug approved?

MS. BENS: I would say no, only because I don't want to think 10 years of my life has not been worth anything. No, I definitely don't think that it's not a success if you don't have a successful drug after interacting with the agency for a number of different years.

I think we can largely take credit for helping to really change the mindset of a number of people within the agency related to the posture that they needed to take on the disease. And in particular, with sarcopenia, that's something that the agency really wasn't recognizing as a disease because there was no actually diagnosed population prior to us bringing it to them.

So I would think that those are wins. I think that, ultimately, our hope is that we will be leading to successfully approved therapies. And I don't think it's a failure on FDA's part if, even after all this time, if they make a call on a drug and they don't approve it, if it's based on the thinking and the rationale that they've put out on either of them.

DR. WHYTE: Okay.

MS. O'DONOGHUE: I would say that, as I said, LLS is not a research organization. And I would say our definition of success right now is just the whole patient engagement aspect. I immediately went there in terms of my prior life. Success equates to drug approval. And I would say, having been with the LLS three years and my experience with the patient-focused drug development, that we have been extremely successful.

I think patient organizations will have great success just in moving the science forward in terms of patient engagement where it's quantifiable

and reproducible, which really is not at all related to drug approvals.

DR. WHYTE: Okay. And we have one question.

DR. SALKELD: Hi. I'm Ellen Salkeld from Aplastic Anemia and MDS International. I don't know if this question will make sense to you or not. But in listening to you talk, I had a question, how important or how do you deal with consensus?

So how important is consensus in this whole process that you're talking about, when we're talking about patients, and researchers, and industry, and everybody having different goals? So can you expand on that a little bit?

MS. O'DONOGHUE: A lot of hard work, and a lot of talk, and a lot of negotiation, and a lot of taking the egos out of it. Seriously. You know, it requires a lot of meetings. And we still, I think, have a lot of work to do in terms of around education because there's a lot of misunderstanding about what we actually mean by patient-focused drug development.

Providers will almost immediately go to the traditional definition of PROs, patient reported outcomes, which is very, very, very different.

So to answer your question, it's just patience and sharing as much data as you possibly can and having repeated conversation around a table. You won't always come to a resolution to satisfy everybody, and I think you have to go in with that understanding as well. In fact, on some topics it may not even be possible to achieve consensus.

Our experience, as well -- and I will leave you speak to it -- our experience as well is that people really who come to the table with patient engagement, they really want to make it work. So they appear to be more open; at least that's been our experience as well.

MS. BEN: And I would say one area where it's particularly important is if you're drilling down in subpopulations of affected communities, I think it's one area where we had the most difficulty trying to reach consensus when we were

going to qualify our functional measures.

Anyone who's been through the qualification process probably knows that a large part of that is determining the context of use that your endpoint is ultimately going to be used in. And getting to what that context of use is, based on what the real information is telling you about the patient that's going to benefit from a treatment that ultimately impacts those endpoints, it is a really hard process.

In our initial letter of intent, it was like the kitchen sink that we wanted the endpoints to apply to, but now we're just at a real small subset of the population. But we're moving forward in a much more effective way.

DR. WHYTE: Good. Well, thank you.

So thank you both, again, for your time.

We just have four more clicker questions, and then I'm going to offer some comments. I asked you two of these questions at the beginning. And the first was how confident are you in understanding functions of CDER and the FDA? a) is

not confident at all, b) is somewhat confident and c) is very confident.

(Audience polled.)

DR. WHYTE: Okay. Well, good.

Next is, how comfortable do you feel about navigating with CDER at the FDA? a) is no idea where to start, b) is somewhat comfortable, c) is very comfortable.

(Audience polled.)

DR. WHYTE: Okay. Who said "no idea where to start?"

(Laughter.)

DR. WHYTE: Come on. All right.

The third is, would you recommend this workshop to others? a) is yes, b) is no.

(Audience polled.)

DR. WHYTE: Great. Well, that's very nice of you.

Then finally, which topic presentation did you find the most useful and learned the most from?

(Pause.)

DR. WHYTE: Jeopardy doesn't count.

(Audience polled.)

DR. WHYTE: Okay. All right.

Well, Rich Moscicki is going to be happy, but lots of good ones.

Closing Remarks – John Whyte

DR. WHYTE: I want to end with some final words and some of my tips. As I mentioned a little while ago, I have a three-year-old and I have a one-year-old, but the three-year-old is very interested in dinosaurs, so it's constant dinosaurs at my house.

I've watched The Good Dinosaur about 20 times and Journey in Time, Land of Time, whatever it is, and there's a dinosaur that talks about wisdoms, and some of you may know that. So I want to give you some of my tips to go home with.

I also want to point out, I think two of the most important pieces in your folder that you all got was the organizational chart of CDER, because many folks have referenced that it's not just going to the commissioner or even the center director, but it's about going to the office and the division

that actually manages your issue. Those are the experts. That's often where the delegated authority is to make decisions. And those are the ones you want to engage with.

As Dr. Woodcock talked about early on, as I've talked about in my prefatory remarks, it is about trying to change the culture. Many of the folks that work here are scientific and technical experts. You might be surprised; most of them are introverts.

So it is a learning process of how to engage with the public. And often when folks come to talk to us, they're angry and they're upset, and we understand that. But it's important to identify who it is you need to talk to.

The other important piece may seem small, but it's our business card. We created these business cards for the Professional Affairs and Stakeholder Engagement Group. And Dr. Woodcock referenced, we can help you facilitate those meetings.

As Bernadette talked about, we've been

working with the Leukemia & Lymphoma Society in preparing a meeting with the FDA, and that talks about creating an agenda and figuring out what's going to benefit both parties.

So I understand, despite this conference and that 2 percent who said they don't understand what to do, I get it. It can be hard to figure out who to talk to. So use as a resource. Use my friends and colleagues at the Office of Health and Constituent Affairs to figure out what to do.

But here are my four tips for you -- they're John Whyte's four tips, not the FDA's four tips -- when you come to a meeting with the FDA. And the first is, know your issue. And it's not, know your issues, plural.

The reason why I say that is often the meetings are an hour. They're an hour. And at the end of the hour, people go on to their next meeting. That's what I learned.

The biggest difference between private sector and government is in government, you meet all day. In the private sector, you only have like

two meetings. So what's really relevant here, our days are mapped out in meetings, start to finish. And what happens is people want to come and talk about five issues. They want to get everything in, in that 60 minutes, and they show 50 PowerPoints, and they speak for 55 minutes, and then at the end they want to have dialogue.

What I think is more important, it's not as if there's a quota. You have your meeting and check box; we're not going to meet with you again for another year, but rather it's about really defining your meeting and the issue at hand. It may be two issues, but no more than that, because people try to accomplish too much. And the main purpose of the meeting is to have a dialogue with the agency.

So again, it's know your issue and really keep your topics narrowed.

The second is to tell your story, and that's one of the things that I learned at Discovery Channel. And I'm a physician and a scientist, but there is the power of storytelling. And one of the

benefits of the patient-focused, drug development meetings is being able to listen to these patient stories.

In our meeting next week with the Leukemia & Lymphoma Society, a big part of that is hearing from patient stories. We don't always get the opportunity to hear from patients, and that's what folks often want to talk about.

We can easily go by email back and forth, and submit journal abstracts, and discuss data, but we often don't get to hear how it impacts people's lives. In the topic of muscular dystrophy, it's important to hear that there might be the 6-minute walk test, but it's more important for a patient to have upper strength mobility so they can dress themselves, so they can feed themselves.

Dr. Woodcock often talks about that patients are experts in their own disease, so don't always look at the meeting as an opportunity to debate data. And we all know that most of the time, data are gray; they're not black and white. They're subject to interpretation. And there is a time and

place for everything, but don't underestimate the power of storytelling, the power of the patient voice and understanding what's important to patients.

The third, I'm always surprised by this, is make an ask. I've been to many meetings, because I've said my day is filled with meetings, and again, people talk for 50, 55 minutes and show slides, and they never ask for anything. They never ask what do you want the FDA to do?

Perhaps that -- you know, some folks are very gentile and very kind, or other folks are somewhat, to be honest, intimidated when you finally get here. They don't actually ask for what they want the FDA to do.

Something that I've been very focused on in the meetings that I help manage and I work with the folks on my team, is really creating an agenda and say, what do the advocates want? What do the patient groups want? And to reconcile that with internally, what does the division need, or what does the division want? And as you're not

surprised, they're often not the same.

So how do we get to a middle ground? But to do that, you have to make an ask.

Part of the reason why this group was created at CDER is also to help educate folks. So when folks come in and they want to talk to us about drug pricing, Dr. Woodcock explained, we don't control drug price.

So it's a good use of time to know what your ask is. If you're going to ask us -- and these are true stories -- to force a drug manufacturer, in a drug shortage of a generic drug, to make that available, the trade at the generic price, we're not able to do that. You know, we don't conduct clinical trials. We don't make drugs.

Cat Chew talked about DDI. We get a lot of phone calls -- I'm not joking -- of people that will say -- and it's always opioids -- that their drug went down the sink and can we send them a replacement. We're not a pharmacy. But that's important to understand what we do.

So you have to make the ask and often people

don't make an ask.

Then finally, it's about follow-up. As you know, the crying baby gets fed. And this is why Dr. Woodcock wanted to create this office. Folks historically will come in and they will often say we had a great meeting. And you know what? There's no follow-up, because everyone has a day job, and much of the day jobs are reviewing applications that are already in the pipeline.

That doesn't mean that your issue isn't important or that it's fallen from the radar screen, but there's lot of priorities here at the center and at the agency, and sometimes you need to prompt us with a general reminder.

But part of my job is to make sure, at these meetings, that we have a plan for follow-up, and that we have that plan for follow-up at the end of the meeting. And Dr. Woodcock is always very focused on that in her meeting, but I recognize she is not at every meeting.

So part of it is understanding. And again, it goes with making that ask. What's the

follow-up, and when is that follow-up? And kudos to the Leukemia & Lymphoma Society who has on their agenda, follow-up. What's going to be the follow-up from the meeting?

You might think these are so obvious, but I've seen over two years how they're often not followed. And those folks that are most successful in terms of getting their position heard, as well as getting agency action, often follow these tips.

I also want to provide my email and my contact information. And if you haven't figured this out already, basically everyone's email here is their first name, dot, their last name, at fda, dot, hhs -- that's what trips people up. They forget the hhs for Health and Human Services, they put FDA -- I know you're taking screen pictures. That's fine.

We're going to put everything online on our site. We're trying to get them up today. It may actually be until tomorrow. So all the slides will be available. But again, that's my contact information, and you should feel free to contact

me, as well as everyone else who spoke today, including Dr. Woodcock. As many of you know, she answers her own emails. She reads her own emails. And she responds to her emails, and she directs her team how to address the issue.

So I hope today has been helpful to you. I also want to recognize Chad, who was out of the room earlier, who really has managed our Jeopardy game and our clicker game, which we wouldn't be able to do without him. So I'm very appreciative of Chad from the center. He doesn't work on my team, but he graciously was loaned to us. So if we can give a round of applause to Chad.

(Applause.)

DR. WHYTE: So again, this is partly a culture change at the agency, of creating this climate of engagement, and it is an iterative process. I don't want you to leave thinking that we have solved everything and that we have moved everything along as well as it should. But I can tell you, as I mentioned at the beginning, it starts at the top, and this meeting would not have

happened. My office would not have been created without the vision and the leadership of Dr. Woodcock to push that we will be transparent. That we will engage with patients.

Again, engagement is about two-way communication. It's not just pushing out from our end what we want you to hear. And it's not just from your end just sending us a note that you need to approve this drug, or you need to take this drug off the market. But it's about dialogue.

So I hope today is the beginning of dialogue for many of us. Again, I want you to feel very open in terms of contacting me directly, contacting any member of our team, having me follow up on issues that you feel you might not be getting addressed. And I will follow up with the appropriate folks at CDER, as well as with Dr. Woodcock.

Again, the slides will be available either tonight or tomorrow. If there are any remaining questions, I'm happy to answer them at the time; otherwise, you're free to try to beat the rush out

on the Beltway.

Are there any questions?

(No response.)

DR. WHYTE: All right. With that, I thank you all for coming, and I hope it was worth your time.

(Applause.)

(Whereupon, at 3:54 p.m., the meeting was adjourned.)