U.S. FOOD AND DRUG ADMINISTRATION

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PATIENT-FOCUSED DRUG DEVELOPMENT

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PUBLIC MEETING

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THURSDAY
OCTOBER 25, 2012

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The meeting convened in the Great Room in Building 31 of the White Oak Campus, 10903 New Hampshire Avenue, Silver Spring, Maryland, at 9:00 a.m., Patrick Frey, Director, Office of Planning and Analysis, presiding.

PRESENT

PATRICK FREY, Director, Office of Planning and Analysis, FDA
DONNA GRIEBEL, M.D., Director, Division of Gastroenterology and Inborn Errors Products, FDA
JOHN JENKINS, M.D., Director, Office of New Drugs, FDA
PATRICIA KEEGAN, M.D., Director, Office of Oncology Products II, FDA
JASON LUNDY, Ph.D., Assistant Director, Patient-Reported Outcome Consortium, Critical Path Institute
GINETTE MICHAUD, M.D., Deputy Director, Office of Blood Research and Review, Center for Biologics Evaluation and Research, FDA

PRESENT (CONT.)

THERESA MICHELE, M.D., Team Lead, Division of Pulmonary, Allergy, and Rheumatology Products, FDA
THERESA MULLIN, Ph.D., Director, Office of Planning and Informatics, FDA
MEGAN O'BOYLE, Patient Advocate, Phelan-McDermid Syndrome Foundation
ANNE PARISER, M.D., Associate Director for Rare Diseases, Office of New Drugs, FDA
JANET WOODCOCK, M.D., Director, Center for Drug Evaluation and Research, FDA

A-G-E-N-D-A

P-R-O-C-E-E-D-I-N-G-S

(9:00 a.m.)

MR. FREY: Good morning and welcome to this initial public meeting on FDA's Patient-Focused Drug Development Initiative, an initiative that is part of FDA's commitments for the fifth authorization of the Prescription Drug User Fee Act that began on October 1st. So thank you very much for joining us for this kickoff meeting.

I'm Patrick Frey, director of the Office of Planning and Analysis in CDER. So the goal of patient-focused drug development is to pursue a more systematic approach for obtaining the patient perspective on the severity of a disease and the current available treatments for that disease.

FDA committed to conducting a number of these meetings during PDUFA V. Each one focused on a specific disease area. You'll hear more this morning from FDA about what it means for a disease area to be the subject of a

patient-focused drug development meeting. You'll also hear more about potential paths forward for patients and patient advocates to advance drug development in disease areas that are not addressed in one of these meetings.

On September 24th of this year FDA announced this meeting in a Federal Register Notice and published a proposed list of disease areas that could be considered for patient-focused drug development. This Notice also opened a docket for public comment on the proposed disease areas. As of last night we have received 438 comments that represent a wide range of disease areas.

The docket will close on November 1st so if you have any further comments after this meeting you'll have a week to get those in. There is guidance in the Federal Register Notice on how to provide comment that is most helpful to FDA as we consider the disease areas for patient-focused drug development.

Today's meeting represents an

additional opportunity for the public to offer input on this set of disease areas. A transcript of our meeting is being recorded and will be available on FDA's website.

After this meeting and the close of the public docket we'll consider your input from these two sources and then publish the list of disease areas to be discussed for the first 3 years of PDUFA V which includes Fiscal Years 2013 through 2017. We will run our second process to identify the remaining disease areas that will be discussed in Fiscal Years 2016 and 2017.

Now, a quick rundown of the agenda. We'll begin with remarks from Dr. Janet Woodcock, director of the Center for Drug Evaluation and Research, followed by a presentation from Dr. Theresa Mullin, director of CDER's Office of Planning and Informatics.

We'll then hear from a panel of FDA representatives who make regulatory decisions on human drug and biologic products that we

review. These individuals will describe their perspectives on this initiative and the proposed list of disease areas that we published in the Federal Register.

After a short break we'll have a period for open public comment on these disease areas. If you would like time to speak please sign up at the registration desk in the lobby if you have not already done so. The number of speakers who sign up will determine how much time we can allow for each comment. We'll make every effort to allow time for those who wish to make a comment. Please keep in mind that written comments through the public docket are just as valuable and useful to us as the oral comments that we hear from you today.

Following the public comment session we have a panel regarding incorporation of the patient perspective in drug development. And this panel will share some lessons learned in their experience in patient engagement and collaboration to advance drug development.

We'll then conclude with a second public comment session on that same topic. There are many disease areas that are actively engaged in advancing drug development for their condition so we encourage you to share your experiences with the group. Sign-up for this session of public comment is also available at the registration desk. And if there's time remaining we'll use it for those who did not get a chance to speak during the first open public comment session.

So I think you've heard enough from me. At this point I'd like to introduce Dr. Janet Woodcock, director of CDER.

(Applause)

DR. WOODCOCK: Thanks, Patrick. Welcome to all of you and thank you so much for attending this really important meeting. I know taking time out of your busy schedules to do this means a lot.

This is a very important initiative that the FDA overtly negotiated within the PDUFA

program, the Prescription Drug User Fee program because we really feel at FDA that we really need to hear the patient's voice in understanding how treatments are evaluated and then what is relayed to patients. Because the patients are the people who are bearing the burden of the disease and they're the ones who really need to know and understand whether a treatment is going to work for them and what type of tradeoffs they have to make with the treatment, because every single treatment has some kind of downside to it.

Right now we don't have a systematic way of hearing from patients and how they feel about their disease. And I think this is a sort of legacy of how medicine has proceeded in the past which is the doctors interpret what the patients say and then the doctors develop an idea of the disease, right? And then they write it up in the medical textbooks and the journals and then that's what the disease is, okay? But fortunately now we have many more tools and

techniques including a lot of IT and so forth that we can actually understand directly from patients.

And there's two things we really need to understand from people. One is what is the burden of disease. How does it burden someone every day and over their time that they are suffering from the disease? And it's specific. Like is it pain, is it lack of mobility, is it trouble thinking sometimes. What is it?

And we know there's a lot of variability in every disease. I'm a rheumatologist so I treat people with rheumatologic diseases. And you know, there's a huge spectrum of any rheumatologic disease from very serious to, you know, something you can live your daily life with, even with the same disease. So what is that spectrum and how do people experience it?

And in any given disease, often for some people, one symptom will be worse or one

limitation will be worse, and in other people, other types of symptoms will be worse. So what is both the range of severity and the range of experience, of personal experience of the disease. And how does that change over time.

And these things are really important for us to understand because when you're thinking of intervening with, say a drug treatment, how the disease changes over time and what symptoms or manifestations of the disease you're targeting are extremely important in designing the trial. Because frankly, if you don't ask about, it you won't know. If you don't follow something and see if it improves or gets worse you won't know whether the drug had impact on that or not. So we want to hear about the burden of disease, what bothers people, what is burdensome, what is progression like in different patients, what is the severity like in different patients. And then we'll talk about the treatments, okay.

Then you can devise ways to measure and collect from all us disparate humans an instrument, say, or something that patients can report their outcomes. Or you can measure something like how fast can you walk a certain distance or whatever. So we have to develop measurable criteria that we can study in people and see how bad their disease is, and then see if the treatment has any positive impact. And all of that depends on how you define a disease. So what you decide you measure. And all that really matters as far as treatments.

And then there is the tradeoff issue, all right. And we also need to hear -- that is really a values issue for patients. We've heard from, for example, the multiple sclerosis community when we had a problem with the drug Tysabri, and it caused reactivation of virus in the central nervous system, and people got very ill from that. We heard from the community, we're willing to take these risks. We want them studied, we want them

described, and hopefully you can get something to prevent this but we're facing a very serious, some of us, prognosis and we want to have access and we want to make those choices ourselves, all right. But we want it as well described as possible. So another part of this whole initiative is really understanding how the patient community with whatever disease, how you look at the tradeoffs.

And we know just like everything else, you know, some people don't want to cross the Bay Bridge, it's too risky, right? So people have different -- each person has a different assessment of risk and how much risk they're willing to tolerate. Other people want to bungee jump off the Bay Bridge, right? So yes, we're all different. So we need to understand that spectrum of risk tolerance and how much you'd be willing to trade off, any given person might be willing to trade off for improvement of various symptoms that they're suffering.

Those things are extremely important. They're subjective. Just having one patient representative who is on our advisory committee or maybe meets during meetings with a company, this isn't going to give us the kind of understanding of the spectrum of the take that people have on their disease because it's not just a single impression, it's a broad set of human experiences that we're dealing with.

And maybe this complexity is why we haven't up till this point done a very rigorous effort to reach out. But I think it's also the fact that now we have better tools, we have IT and other tools that we can actually collect this information and utilize it.

So I'm afraid that because we agreed as part of the negotiation, right, to do 20 diseases that there's going to be excessive focus on, am I on the list, is my disease on the list. And I would urge you not to do this. It might have occurred to you there are many,

many more diseases that afflict us as humans than 20. And so what these are is kind of a sample and hopefully we'll pick diseases that we have poorly defined understanding of the disease and we can work our way all the way through it.

But I think what this sample will do is help us figure out how to do this more generally. All right, how is this done. How do we get this input from patients and how do we set our standards for the disease based on really the patient input for benefit and for risk.

Now, these efforts I think will go on over 5 years and we have already done something, for example, in the obesity space over the last year where we met with a variety of patient advocates. We also met with treating physicians for obesity and so forth, and we learned a great deal I think about how that disease looks from the patient point of view versus say the community or the treating

physician point of view or so forth. And I think that really gave us a great deal of insight. Right now we're working with the chronic fatigue syndrome community because they don't have any drugs to treat their diseases. And we're talking to them about how we could better understand and measure the symptoms in chronic fatigue. So this process even if whatever disease you have or represent isn't on the list of 20 very much can be done.

And please don't underestimate the power of patient and patient advocates to make a difference in the disease. We have some outstanding examples out there in the community, cystic fibrosis, multiple myeloma foundation, many others who are already doing these types of things.

And Anne Pariser who's going to be on the panel later has told me about two mothers who have collected natural history data on patients with a very rare disease using the power of the internet. And actually has probably

collected according to her maybe more information than ever existed on that disease that has been put together. So, this can be done and we need to learn together how to do this. And that's what the 20 diseases are going to be about. But we have to go much beyond that because there are many more than 20 diseases that afflict people.

So, but the ones we would pick for this we want to pick diseases where really maybe the progression might be unclear. We don't have good endpoints. There might be a lot of tradeoffs involved in the toxicities. And so we get all the range of the issues that we're going to have to grapple with. Maybe they don't have good endpoints for the disease, maybe they don't understand the natural history whatsoever. Maybe there are only patient-reported outcome measures that could be used in that disease and so forth. So we want ones that would provide us with really exercising our brain.

But I would encourage everyone to participate with us, whether it's about your disease or not so that you can learn. Because if we're going to be successful in this it's really going to have to be the community that does a lot of the work. The FDA only has a very small handful of people, right, and we do many, many different activities. And so it's really the job of the researchers and the community at large I think to carry this forward. And you can do it, it can be done and we can really make a difference in how we understand the patient experience both of disease and of treatment which is what we need to have.

We need to have insight into what it is like to have that disease at a moment and over time and what are the consequences of having an intervention, like a drug intervention. What does that do both for good and what are the negative aspects of that. And how would you trade those off.

So, FDA doesn't develop the drugs.

We review drugs that are sent to us for safety and effectiveness. And we don't do the research. But we set the standards and that's one of our major jobs. What do you have to study to get a drug on the market. And so that's really what we're talking about here. How do you study these drugs in each different condition. What is the proper evaluation method. So our job really is to set these standards and then review what we get submitted to us against the standards. But it turns out that setting those standards requires a tremendous amount of input.

So, in summary, this is an experiment. I think we're turning the page to a new way of involving patient and patient groups in drug development. It's going to be an experiment. It's going to have its ups and downs like anything new. But please bear with us and hang in there, because I think the patient community is the one that can make the difference here. That's who we want to hear from and those

folks are going to represent the authentic understanding of the experience of the disease and the experience of treatments of a disease. So thank you very much for coming today and for your input. We will all stay in touch as we move through this process. Thank you.

(Applause)

MR. FREY: All right. Thank you, Dr. Woodcock. We'll hear from Theresa Mullin on FDA's Patient-Focused Drug Development Initiative.

DR. MULLIN: Thank you, Patrick. Good morning, everyone, and thank you for coming. Sometimes people at FDA are thought to be inconsistent by people on the outside, and I think what you're going to see is a great deal of consistency between what Dr. Woodcock just said and in my slides. So hopefully not to make it seem too much the same, it also shows that I do listen to my boss and basically try to carry out her vision and her ideas for what we could do, which really was part of the impetus

for us to get this explicitly into the PDUFA agreement.

And so as she said, this effort is driven in large part by some basic observations about the patient's role in drug development and in even assessing the benefits and risk. We need to assess, as part of benefit-risk, the severity of the condition and the current state of the treatment armamentarium, and patients clearly with the disease have a direct stake, have the ability to report on the disease and the effectiveness of the treatments in a way that no one else can.

And so they have a really critical piece of input to provide and help give us some greater clarity and insight in looking at the analysis of the severity of the disease condition and the current treatment options and how well they work. And based on that it's clear that if we could have a more systematic approach to trying to obtain the patient perspective that would really help illuminate our assessment of

benefit and risk.

And this is just an overview of the benefit-risk framework that we've been developing and will continue to develop and expand in PDUFA V. We have another commitment related to that. We had already planned informally ourselves to commit to this but this allows us to have a little more resourcing and a little more explicit public commitment related to it.

There are five considerations. The first two, the analysis of condition and current treatment options, really provide the context for how much risk FDA understands would be acceptable and that we would consider to be acceptable to expose patients in exchange for some benefit. And that doesn't need to be done anew every time that you look at a new drug application, that's really related to the disease conditions. And so that's where we see the ability to inform those first two rows, if you will, of this table, that we put together

for a particular application to examine it by getting input at the disease level from the patients.

The other pieces of this framework, benefit, risk and risk management, incorporate the expert judgments of the reviewers. And clearly there's an objective component to this, there's the scientific data, there's the experience of the reviewer and their expertise in their field. There's clearly a subjective piece to this, there has to be. The data that we receive is not complete. There's always some uncertainty about the information about the data, and how well the drug will work in the indicated population beyond the clinical trials. And the same is true of risk information that we receive. We have to extrapolate and think, what's that going to be like when it's on the market, and the drug's used for a longer period of time, and so on. So there's naturally some bit of subjective judgment in there by necessity. And I think

we'd probably all want it to be in there too. I don't think we want this to be too algorithmic.

So talking a little bit more about the analysis of the condition. Questions that we identified, and you may have others that you'll tell us we ought to be asking as well, but certainly in thinking about what would we really benefit from hearing more about from the patient's perspective, are questions like some of the ones that Dr. Woodcock mentioned, and I may be repeating some of them here, but what are the clinical manifestations of the disease that have the most impact on patients.

What other aspects of the disease really impact a patient's life affecting mobility, sleep problems and others. We've heard patients come and tell us about, for example, I remember a Parkinson's disease advocate saying that sleep problems are very significant for Parkinson's patients and that wasn't being adequately captured.

How do the clinical manifestations

change over progression. Again, that's something we need to hear firsthand to better inform us about that from patients. And what other aspects of the disease change over time.

These components, if they're addressable in a systematic way in trials, may turn into other aspects of measurable benefit that could be used to show a drug works. And that's very important because whether a drug works is the primary consideration in whether or not it's going to be approved and if we're going to expose patients to any sort of risk.

And then the current treatment options: here is an example of questions that we'd really want to hear more from the patient's perspective on what you perceive to be the current standard of care.

I had a presentation at a meeting on Tuesday and I made a comment that this seemed to be something that mostly the physicians would speak to, and a mother of a patient with a rare disease came up to me and she said, now I think

the patients have a lot to say about this too, and their families, because people that she had talked to who had the same disease as her son and others in her family, said that there was no consistent standard of care, that everywhere that these people were being treated, there was some other standard that a doctor said was the standard, and no consistency at all. So patients have a lot to tell us about whether there's a standard that they're experiencing and is it truly a standard. And that would be helpful.

What therapies are being used to treat the condition today, whether they're approved for that indication and whether they're non-pharmacologic as well as drugs. And how effective are those therapies in treating the clinical manifestations of the disease, and how well do they mitigate other problems, other aspects of the disease that impact a patient's life. How well tolerated are they, does their effectiveness change over time with progression

of the disease, how effective are they in subpopulations and other questions that you will help us identify I think.

This initiative under PDUFA V really gets us a little bit more resource to support it and we've made a commitment to these meetings. I think we'll get a couple of benefits from having these meetings.

One of the things as Dr. Woodcock indicated, we may hear of a need for other instrumentation, for a patient-reported outcome tool, and that's something that will take a little bit of time to develop. Anne Pariser might be talking a little bit more about the various things that can be done. I don't know what her talk is going to be today but I know I've spent a lot of time trying to talk with her and coordinate, make sure I'm on the same page with Anne in terms of what can be done. But that's one approach.

We also think these workshops will produce a report that by itself will have value

and be useful to reviewers. And our aim is to make them very useful.

And so we started to launch this PDUFA V effort with the four meetings per year in different disease areas by collaborating with the Center for Biologics and coming up with a starter list of here are the areas that we think we really could use additional information. We don't have perhaps as much good measurable information today about patients' experience with the disease and the burden of disease, and have published that.

With the input we get today, we think we won't go and map out the next 5 years. It would be in the nature of this being an iterative effort, and trying to learn actively along the way and share our learnings with you along the way about what works well. So we'll try to identify diseases for the first few years and then initiate another process to determine what to take up through this formal process.

Beyond that, this formal process

doesn't preclude other meetings. A lot of the review divisions in CDER have told us that they already have other meetings, a lot of other meetings underway and planned. In some cases they have asked us what questions we're using. They may incorporate them into their other meetings. And so we see this as being not a rigid thing, at least 20 meetings over the 5 years but we anticipate there will be other venues and ways that we'll be able to do this going forward as we try to get this information in.

So today's meeting is about hearing from you on that preliminary list of our nominated disease areas and also to comment through the docket about both the list and our approach to doing this and collecting this information.

Here are the criteria that we used. We nominated diseases from a wide range of areas. Generally we asked reviewers to identify diseases that were chronic, symptomatic affect

the functioning and daily living of patients. Were there important aspects of the disease that they could say were not well captured, or formally captured in clinical trials based on the guidance we have today, for example, perhaps, or what we get in submissions from sponsors.

The diseases we asked for would represent a range of severity and if there were potentially -- if there was a disease with an identifiable subgroup that had particularly severe impact, we were interested in including those in this list. And also just looking at broad population impacts. And also diseases where there are no therapies today and we don't have information about how it directly affects how patients function and feel.

This is the preliminary list that we identified. And I'm sure you probably have this. I'm not going to read this list to you. It's been in the Federal Register for over a month. And so that's our starting list.

And just to review some of our key objectives for this effort: we do want to get broad patient input, and so we're facing questions like, who represents the views of patients. In trying to begin to ask these questions, I have to say we've gotten some very helpful email input and input to the docket.

One of the themes of those submissions to us is that patients feel that they have a unique voice, and that they have something to say that patient advocates who are not as close to the disease. I mean who care about the disease but maybe don't have the disease or can't represent the range of views, can't replicate or speak for them, that patients have told us in the submissions we've gotten so far that they need to be able to tell us directly what they think about the disease and answer these questions.

And so we have to say what kind of input -- who represents patients. How do we ensure that we're getting the input from

patients and getting truly their perspective on that. That's a challenge for us with process.

We want to use formats to collect this that are effective and by that I mean we want to faithfully capture what the patients are saying, not paraphrase it, not have it come across in some way other than just the way they meant it, and that we represent their views transparently.

At the same time we need to make this useful to reviewers. So we need to communicate that then in a form that's usable to the reviewer, that if a reviewer gets an application for a drug in that disease area that the information that we provide is providing some valuable insight, something useful to them. Otherwise I think we'll all feel this isn't a good use of our time. So that's very important to us.

The document that comes out of each of these meetings, I want that to be very useful

to the reviewers who are going to then be looking at it later.

And we're also trying to balance making sure we maximize access to patients and we have reliable venues for collecting this information. Balancing the in-person collection of information with electronic and making sure that we again emphasize accessibility and the reliability of those approaches. And also the other considerations I mentioned: are we getting true patient views and so on. So those are our challenges.

And I'm so gratified by the enthusiastic interest and response that we're getting, because we're going to need patients' help in trying to figure out how to do this well. I think we're all very interested in doing this well and getting the most valuable information we can to advance our ability to review applications and to get drugs developed to treat diseases that people are experiencing.

So with that I just want to say thank

you for being here today and thank you in advance for your help over the next several years.

(Applause)

MR. FREY: All right, thank you, Theresa. I'd like to invite the first panel up to the front table.

So we've asked this panel to really consider the Patient-Focused Drug Development Initiative and what it means to them, what it will mean in PDUFA V and what it will mean potentially beyond PDUFA V as well.

We have a number of division directors here as well from the Office of New Drugs. I'll let them all introduce themselves as we go through the panel. So these are the individuals who at least in their therapeutic area identified some proposed disease areas that are included in our preliminary list. We've asked them to share their perspective on why those disease areas were nominated as part of patient-focused drug development.

So I think we'll begin with Dr. John

Jenkins.

DR. JENKINS: Good morning, I'm John Jenkins. I'm the director of the Office of New Drugs in CDER. And for those of you who may not be that familiar with our structure my office involves all the review divisions for all the therapeutic areas. So there are 18 divisions in my office that are organized around therapeutic areas.

So for example you'll hear in a few minutes from Dr. Griebel, who heads up the division that handles gastrointestinal and inborn errors of metabolism diseases. So that's the way we're organized, around therapeutic areas much like medicine is organized.

And in each of those divisions we have experts in those therapeutic areas. So in our cardiology division we will have experts in cardiovascular diseases as well as nephrologists because they also cover diseases of the kidney and hypertension and things like

that.

So that structure is very important to help us in managing our task, which is to weigh the benefits and risk of drugs all the way through development and into the marketing period and in the post-marketing period, to always be making decisions about whether the benefits of those drugs outweigh their risk for the population of patients that they're intended to be used in.

I think this initiative is going to be very important to us because it allows us to hear the perspective of a patient community affected by those diseases. As Dr. Woodcock said, each individual patient affected by a disease is going to have very different perspectives maybe from their colleague who has the same disease, because everyone has a different manifestation of the disease, a different impact on their life. Everyone has a different tolerance for risk.

So I think what's going to be most

useful for us is to kind of hear the overall perspective of the patient community so that we can factor that into our decisions as we're overseeing the clinical trials that lead to development and approval of drugs, we're making decisions about which drugs get approved for marketing, which drugs don't get approved for marketing.

And then very importantly in the post-approval area, when new safety concerns come up about a drug, those often get a lot of public attention. And often the patient perspective of those people who are benefitting from the drug get drowned out by the safety concerns of the safety advocates.

And I think one of the things we learned in the PDUFA V negotiation and stakeholder process is you get very different perspectives about drug benefit and risk when you talk to patients and patient advocates than when you talk to consumer advocates or people who don't have the disease.

There's a very different focus, in my experience, when a drug gets on the market and starts having a safety problem identified, that maybe wasn't anticipated or is occurring at a higher rate than expected, often the patient voice of those who are deriving benefit is drowned out in the media and the public perception of the drug as we evaluate that safety concern.

So I think it's going to be very important to always be able to re-balance those discussions by understanding what is the impact of this disease, what risk are the patients willing to accept for the tradeoff of the benefits that they are deriving from that drug, and to bring that perspective into the equation.

We think we capture that in our decisions, but I can tell you it's always going to be useful for us to have a formal mechanism that we can refer back to and point to, these are the adverse events of this disease on the patient with the disease.

Just as an anecdote, a few years ago we had, as you may recall, some significant safety discussions around drugs for the treatment of asthma. There were some concerns about whether the bronchodilators that we use to treat asthma might actually paradoxically make the disease worse, and might actually in some people lead to their death from that paradoxical response. A very serious safety concern, one that we took very seriously, but we also look very carefully at the benefit of those drugs to patients with asthma.

I'm a pulmonologist by training, so I spent my early career taking care of patients with asthma, so I knew the impact of those diseases on the patients and the impact from not being able to sleep through the night, not being able to go to school, go to work, not to be able to swim or do your sports activities. So I was very aware of the benefits of those drugs on the aspects of the disease that were very important to the patients.

In the discussions though about the safety concerns, I realized that some others who weren't as connected to the disease tended to minimize those benefits. So in their eyes, the fact that a very small number of people might suffer a serious adverse reaction or might die could never be outweighed by the fact that a large number of people were able to sleep through the night, or were able to go to school, were able to work, were able to breathe. So it became kind of an example of how you can get very different perspectives coming to the table when you're discussing benefit and risk related to a drug.

And at the end of the day all the decisions we make are about benefit and risk, and they require judgment. So you always have to weigh the science, the information you have in front of you, but you also have to use judgment in deciding whether the benefits outweigh the risk for the population of patients who are likely to use that drug. So I think having

perspectives from the patient community in a more formal way is going to be a very powerful tool to help us not only drive drug development in ways that will address the impact of the diseases on the patients, but also provide that balance when a safety concern is being addressed, about how important is it to sleep through the night if you're asthmatic, and how willing are you to accept that small risk that you might have an adverse reaction of your asthma actually getting worse.

Sometimes in these discussions I'm reminded of the movie Rain Man. And most of you look like you're old enough to remember the movie Rain Man. But if you recall in that movie the title character needed to get from Cincinnati to California. And he wanted to fly Qantas Airlines because Qantas had never had a death from an in-flight accident. And in his mind that made perfect sense. But of course Qantas doesn't fly from Cincinnati to California, so it wasn't a practical view of

the world. So I think that's where you can bring in some more of that practical view of the world about the discussions and the impact on patients to help us make what are very challenging, often very controversial and difficult decisions that are based on benefit and risk.

You'll hear from a couple of my division directors about how they view this initiative and how they selected the diseases that they put forward, but hopefully that will give you some overall context for how we're looking at this initiative in my office. So thank you all for coming.

(Applause)

DR. GRIEBEL: So you already heard who I am. I'm Donna Griebel. I'm the director of the division that manages the gastrointestinal drugs and the drugs for inborn errors of metabolism. In addition, we manage the applications for the TPN which is total parenteral nutrition or intravenous nutrition for people who are unable to take in nourishment

or adequate nourishment by mouth.

You just wanted us to run through introductions right now?

MR. FREY: And share your perspectives.

DR. GRIEBEL: Oh, share my perspective as well. Okay. Well, I would just tag onto what Dr. Jenkins said. I'm in a division or managing a division for which I am not a gastroenterologist, I'm not a geneticist, I'm trained as an oncologist. So I walked into a division with multiple drug programs under development for which I was not trained and did not, like Dr. Jenkins, have the experience of being the clinician who managed the patients who were actually experiencing the disease.

So I would look at what we were using as endpoints and what the assessment tools were and ask, why are we using this? How does this apply to patients?

Many of the diseases in our division are -- there are not real objective measurements

in terms of doing a specific test to determine how a drug is affecting the disease. They are symptomatic diseases in which the patient is the holder of all the knowledge of how the treatment is impacting them.

And what I found was that many of our tools were tools that were developed by clinicians. So it was the clinicians' perspective on what was happening with the patient. And some of the tools just didn't make sense.

And when you questioned further, you found that they were developed on the back of a cocktail napkin and by some very prominent physicians who do have the good perspective because you are seeing patients from a day-to-day basis, but I wasn't clear what really was important to the patients.

So when we set about picking the diseases that we would embark on in this program, they were diseases for which we have had drugs developed, but as science has advanced the

treatments have become very sophisticated and have some significant toxicities. And when you are providing patients with therapies that can be highly effective but come with it a lot of toxicities that over the years can be quite devastating, and we've heard about that from patient advocates at advisory committee meetings, it becomes very, very important to know that you are impacting the thing that is most important to patients when you say that the drug is effective, that it is effective on something that is meaningful to patients. So it was very difficult to pick two specific disease areas when we are a division full of many, many diseases. And I think most of the review divisions have that same problem. But that's the approach that we took.

I know Dr. Woodcock says you can't effectively address this with just one patient voice at meetings along the way, but we have made every effort to try to systematize bringing patients into the development program of

different drug products so that we can hear the voice early on of at least a patient.

And we have had experience where we have had companies who have made every effort to go out and find out from patients what is important to them on some really difficult symptomatic diseases, for which there are no therapies.

And we've been presented information that they have come back to us with from these meetings, and we sometimes have been confused about what we're hearing and we don't understand specific data that came back to us from talking to patients.

We have worked with OSHI to actually set up teleconferences with patient groups to follow on, to query more about what, on a specific issue, what did you mean by this, and what specifically about this is troublesome, so that we can better understand how we should be building the endpoint for the clinical trials.

So just echoing what you've heard I think from the presenters today, that just these two specific meetings from my division is not the limit. We understand that we need to hear the voices in every disease and we are making every effort to do that in every means possible.

(Applause)

DR. KEEGAN: I'm Patricia Keegan. I am the director of the Division of Oncology Products II. And while I'm representing my division, I'm also sort of more broadly representing the Office of Hematology and Oncology Products, which consists of three clinical divisions, which review drugs for the treatment of hematologic cancers and benign hematologic conditions like sickle cell and amyloid and a whole variety, the Division of Oncology Products I, which focuses on breast cancers, genitourinary cancers and ovarian cancer, cancers of the GYN system, and then my division which has basically all the other solid

tumors, a really heterogeneous group of thoracic, head and neck, gastrointestinal malignancies, brain tumors, pediatric tumors, et cetera.

And I want to say first off that the Office as a whole and its many iterations -- we've gone through, I think I've gone through about five or six reorganizations in my time at FDA, but always with the review of cancer products -- that we have a long history of involvement of patient advocates, working through the Office of Special Health Issues to involve them in end of phase II meetings for particularly unique development programs for efficacy trials or in our advisory committees, and also for products that don't go to an advisory committee but where a decision on a new drug approval or new indication may exist, we often seek advice from a member of the advisory committee or a member of the medical oncology community and a patient advocate who are cleared as special government employees.

So we have had that relationship for a long time. However, we've not been able to utilize it as fully as we might like, particularly for meetings with industry or for those drugs that don't go to advisory committee, primarily due to time constraints, or resource commitments. And we hope to be able to work through streamlining the process so that we can more fully utilize it.

In identifying the kinds of areas that we would like to work on in the Office of Oncology, the three clinical divisions worked independently at selecting which areas were of interest to them, looking at the considerations. And so it was a lot like the blind men and the elephant. We actually came up with a very different approach towards which areas we would seek patient advocate input.

The Division of Hematology Products decided that where their greatest needs were in the development of good patient-reported outcome tools were in areas of chronic disease

that affect daily living where we can measure changes from drug treatment, but we don't really know if those changes are actually having an effect on patients' lives.

So they selected areas like sickle cell disease, chronic graft-versus-host disease, amyloidosis, aplastic anemia, areas where we can measure effects. But the question of what those effects mean, and were they really important to patients, and were they representing significant improvements, is one that's challenging for them. And so their hope is in moving forward to develop better patient-reported outcome tools to really inform our decision-making when we're looking at a new drug: is this really something that patients need and want and will change their lives.

With regards to my division, what we did was take a different tack. We selected two diseases as model systems that actually covered several of the considerations that were on the table. Those considerations were areas

where the aspects of the disease aren't really well formally captured. And in part that's because there's no dominant symptom, there's no one unique defining symptom for those diseases that we can rely on.

And we have a difficulty in determining how to weight different symptoms from different sites of metastasis, for example, and come up with one way to measure how symptomatic changes might benefit patients because it's so heterogeneous.

Another aspect that we hope that these diseases would model is the idea that there's a broad range in terms of the size of the affected populations. These are two diseases where drug development has been quite varied. For instance, in lung cancer we made very broad distinctions. People either have small cell lung cancer or they have non-small cell lung cancer, which is 85 percent of all lung cancers.

Well, that's no longer even

considered an orphan disease. But now with the advances of genetics, with identifying drugs that seem to work uniquely in other histologic subtypes of those cancers, we're jumping back and forth between non-small cell lung cancer, only those that are ALK-positive which is 5 percent of those.

And we're having these -- the same drugs are being used to treat both the big populations and sometimes the small populations. And we're needing to determine how to move from that really big category into the small categories where there's not many patients who are available for evaluation, and still being able to make the kinds of assessments of benefits and evaluation of risks that we need to make approval decisions. So, we're going to need to figure out new ways to look at this in order to be able to get the right data and still serve those small, tiny populations.

And then I think the other is that these are two of our most active areas of drug

development. The genetics and the genetic understanding of the disease is really coming together with a lot of the drug therapy. So it's an area that's very ripe for looking at tools or new endpoints. Because we have more trials, more drugs, more things to look at.

Not that all of our disease areas aren't moving forward, but these two in particular seem to be very hot at the moment and so it's a good area in which to investigate and get input that we hope we'll then be able to bridge back to other diseases that have similar problems, other cancer subtypes. So that it's not that we're focusing only on these, but that this is a unique set of circumstances and we hope that we can take what we learn here and bring it into other areas.

The third division which has, as I said, breast, genitourinary, and GYN malignancies, are areas where first we have a fair number of drugs and effective drugs where there's less of the issue about disease

progression where it's not as much built into smaller and smaller subsets.

And they chose to focus more on patients' considerations when there are vulnerable populations. So they selected areas to look at as cancer in young patients, cancer in pregnant women, cancer in sexual dysfunction, and cancer in depression, really to look at the issues of vulnerable populations and risk tolerance, and how should we be assessing differences in risk tolerance in these somewhat unique situations: small, vulnerable populations which aren't necessarily limited to the diseases that they look at but again could be more broadly applicable across both all solid tumors, all hematologic malignancies, but a different kind of approach.

So we took actually unintentionally different approaches, but it just turned out when we turned in our list, they were all somewhat different. And we think that across the three divisions, that will allow us by having

taken different pieces of the pie to have a broad chance to look at many aspects division by division and hopefully be able to apply that across all three divisions to advance the entire field of oncology.

(Applause)

DR. MICHELE: Hello, I'm Terry Michele and I'm here representing the Division of Pulmonary, Allergy and Rheumatology Products. Our division covers diseases of the lungs, allergic and immunologic diseases as well as all of the rheumatologic diseases such as lupus and rheumatoid arthritis.

In our area we have a large number of diseases that are severe and life-threatening, many of which represent areas of unmet medical need. And that's why we're so excited about this initiative because patient input in these areas is just so critically important to what we do. Many of us in the division still see patients because we feel that it's important to stay in touch with, you know,

why do we come to work every day.

And in our division for the majority of these disease areas, we do have some form of ongoing clinical trials and some endpoints that we're working with for drug development. So we chose to nominate an area for which we have virtually no ongoing clinical trials and no endpoints that we have validated that we feel work in this area, and that's chronic fatigue syndrome.

This is a complex and debilitating disorder that's characterized by profound fatigue and that's not improved by bed rest and may be worsened by physical or mental activity. And the symptoms often result in a limited ability of patients to participate in daily activities. They're very variable from patient to patient in number, severity, type and so that's why we feel that we really need to get a broad input from patients in this area.

Again, because of that, clinical trials are very hampered because we don't have

endpoints and we don't really even have a good definition of the disease. So, that's why again that we would like to help delineate a pathway forward in this area and why we chose it.

Again, we recognize that there are many diseases and we agonized a bit over this list because there's so many areas that we would really like to put patients' input. And we welcome patient input in all of these areas. So whether or not a disease is formally chosen as part of this patient-focused drug development program, we in our division very much encourage feedback from patients and advocates.

And you'll hear later on about mechanisms that you can use as patients and advocates to interact with the FDA whether or not you're on this patient list. This is as you heard just a pilot and a way of beginning to jumpstart the process.

With regards to chronic fatigue syndrome I'd just like to mention a couple of specific resources that you can provide

feedback, again, regardless of whether or not the disease ends up ultimately in this program. One's the Chronic Fatigue Syndrome Advisory Committee at HHS to which the division provides an ex officio member. And we're very open to hear feedback at that meeting.

We also have ongoing efforts to involve patients and there's an open docket on the FDA website. So if you just type in "chronic fatigue syndrome" you can provide feedback about this illness. And we'd encourage patients with other illnesses to also come to the division because we're very interested in what you have to say. Thank you.

(Applause)

DR. MICHAUD: Good morning. My name is Ginette Michaud. I'm here to represent the Center for Biologics Evaluation and Research. Our center has two offices that regulate therapeutic products, one of which is the Office of Blood Research and Review of which I'm the deputy director. Our office regulates

transfusable blood components, plasma-derived products and their recombinant analogs.

And the other product office that I want to mention is the Office of Cell Tissue and Genetic Therapies, that deals with stem cell therapies, cord blood for example, and a variety of tissue and genetic therapies.

Our center nominated a number of candidate disease areas for consideration at today's meeting and we really welcome this opportunity to hear patient perspective on this preliminary list. We also of course want to hear your comments on the criteria that were used in selecting these candidate disease areas.

The disease areas that were put forward by FDA include six from the Center for Biologics including clotting disorders, thrombotic disorders, primary immune deficiencies, neurologic disorders that are treated with immune globulins, hereditary angioedema and alpha-1 antitrypsin deficiency.

Now, while we nominated these six

disease areas I want to emphasize that we also have an interest in a number of the other disease areas that were nominated as candidate disease areas. And so we will be very attentive to the input that the Agency receives at today's meeting.

Why we selected these diseases is directly related to the criteria that were put forward by the FDA. But most importantly these are areas where we really do seek public input. Tracing these selections back to the criteria let me mention a few of them that were relevant in the selection of these disorders.

These are for the most part chronic diseases that are highly symptomatic, and where the symptoms can be quite debilitating and in fact even life-threatening. These are disorders where the symptoms have a real impact on patients' functioning and on their activities of daily living.

You will note also from this list that for the most part these are rare disorders,

and of necessity the clinical studies that are conducted in support of the marketing applications tend to be smaller, much smaller than typical drug trials. And what we often have are studies that are focused on one outcome, one patient outcome, and it's not always clear that those are the outcomes that are most relevant to patients. And so this is another reason for the selection of these disorders.

We've heard about also the importance of selecting disease areas that have a severe impact on certain subpopulations. And I would just note that for a number of these disorders there is a severe impact on pediatric populations. So therefore this also supported the selection of these disease areas.

I want to really emphasize that we can benefit in our assessment of new products from hearing patient perspectives on -- as you've heard earlier from other speakers –- your perspectives on disease severity. What matters most to you in terms of future treatments

and what are those gaps and unmet needs in existing therapies.

And very importantly, and this has been mentioned by others, what do you consider to be a tolerable risk when we decide to approve a clinical study and say that a clinical study can go forward for new therapy, but also ultimately when approving new products.

Now, the Center for Biologics will be conducting 3 of the 20 planned public meetings that are going to be focused on these selected disease areas. We recognize that we can't tackle all the disease areas of interest in the next 5 years, but this is a start and we're starting on a path of I think greater and more systemic consideration of patient perspectives.

And we really need your help today in helping us refine our list of candidate disease areas and the criteria that should most account for -- should be most significantly considered in deciding on a final list.

I just want to close by saying that

today's meeting is very much in the spirit of the many interactions that the Center for Biologics has had with patient groups over the years. And we recognized many years ago the value of these interactions in understanding your concerns and in encouraging the designs of studies that are consistent with patient needs and that have hopefully patient outcomes that are relevant to patients' lives.

And we have in fact been successful in some instances in even involving patients as consultants in the pre-market application review for certain products. And this is something that we would be very much interested in continuing.

We have engaged patients on our advisory committees, patient representatives. We've had patient group representatives speak at our scientific meetings, at our workshops. And these are all activities that we see as being highly valuable and that will continue in parallel to this initiative.

So we hope that today's meeting will foster continued interactions with patients and patient groups, and that it will be a launching point for a more systemic or systematic I should say approach in obtaining patient perspectives on disease severity, on unmet needs. And ultimately this information will help inform our benefit-risk assessments and support FDA's decision-making when it comes to clinical trials and the approval of new products. So thank you very much for your input.

(Applause)

MR. FREY: I just want to say thank you very much again to this panel for sharing your perspectives on this initiative. I think this has been very informative to hear what you have to say about the disease areas that you put forward.

We're going to move to a short break and try and get back here by 10:15. We have a little bit of planning work for the public comment session so if you can be back in your

seats in about 10 minutes that would be great. Thanks.

(Whereupon, the foregoing matter went off the record at 10:06 a.m. and went back on the record at 10:19 a.m.)

MR. FREY: All right, so for anybody who identified themselves as wanting to make public comment during this session, we have your names on three slides here. And I'll just slowly go through these if you can find where you're located.

We have one mike in the room. And to make this run fairly efficiently, we'd like there to be at least a small line at the mike so that we can click through this and makes sure that everybody gets a chance to speak.

We had some late registrants as well. We anticipate having time in the second comment period that we can use from the few people who identified later that they'd like to speak. So that's slide 1. There's slide 2. And there's 3. Hopefully you're able to

find yourself.

We have a timer up where I'm sitting so that each speaker will be given 2 minutes. It'll be green for 1 minute and then yellow for 1 minute. And that's really so that we can make sure that everybody who wants to speak has a chance to speak.

So the for first comment, consistent with the FR Notice one comment was submitted requesting a special accommodation. This individual is Scott Johnson and I'll just read what he submitted.

"On the October 10th meeting with FDA, the patient consultation meeting, I heard an FDA official state that the FDA did not include ALS in the initial list of 39 diseases because it already understands the need and knows the priority an ALS treatment or cure deserves.

No one has ever stated that ALS didn't meet every single criteria for inclusion. ALS does. Approving a safe and effective ALS

treatment or cure should be the FDA's ultimate primary goal, but there is more to understand about the disease than its invariably fatal nature.

My name is Scott Johnson and I have ALS. My ALS is unique and unlike any other. It will not progress exactly like anyone else's. I was diagnosed in June 2009 and had symptoms in early 2008. Others diagnosed with ALS after me have already lost their voice, ability to breathe or life.

Unlike many other diseases, my life expectancy cannot be measured down to the exact number of months. Changing my lifestyle will not improve my health, nor is there a chance of remission or survival with treatment. The chronic pain I experience in my joints and limbs has been ignored and gone untreated by my care provider since it started about a year after I was diagnosed.

As my disease progresses, there is less and less the medical community can offer

me to make my journey comfortable in terms of drugs without risk of liver damage, addiction or difficulty breathing, risks my doctors, not me, are unwilling or unable to expose me to. As a consequence, I have been told to expect to live with my pain until I'm ready for hospice.

As my breathing goes, so go the options for many basic types of care and treatment, life-saving and routine, unless I decide to get a tracheotomy. If I get a tracheotomy I essentially commit myself, my caregiver and my family to what could amount to years of additional care and a huge financial burden from the additional medical costs.

Of course, there is no treatment or cure for ALS so the end state is currently predetermined, typically death within 3 to 5 years of diagnosis.

I provide that short summary of my ALS story to show the FDA that they may still have something to learn directly from ALS patients. ALS is obviously a complex disease

with the potential for many secondary issues like the one I described. The only way the FDA is going to really understand the entire ALS disease process and the unmet medical need is by talking to ALS patients and caregivers directly.

The only way the FDA will really understand the risks ALS patients are willing to accept in drug development is by talking directly to ALS patients. I encourage the FDA to change its position, add ALS to the disease list and make ALS the standalone topic of the first PDUFA V patient meeting."

Thank you, Scott. Our next speaker will be Jan Wolf from the National Alopecia Areata Foundation.

MS. WOLF: Good morning. I'd first like to say thank you for having us here today at this important Patient-Focused Drug Initiative.

The first thing you probably notice about Ashley and myself is that we don't have

any hair. We have alopecia areata. It's the most commonly seen non-infectious hair loss disorder in children and it can affect the psychological well-being of us.

There are over 5 million people with alopecia areata in the United States. It's an autoimmune disease and it results in the loss of hair on the scalp and elsewhere on the body. It can progress from patchy alopecia like what Ashley has to myself which is the most severe form, which is alopecia universalis. I have no body hair whatsoever.

This process is very individualized and there are some off-label treatments that are available but it depends on the extent of hair loss and the person's age. The results are often unsuccessful, disappointing and there are many unwanted results from some of these drugs. We desperately need an FDA-approved treatment.

Lack of eyebrows, eyelashes can cause eye irritation. People often mistake our

identity because of it. It affects children and adolescents. It leads to loss of self-esteem, loss of self-confidence, can lead to stress, anxiety and depression, and in severe cases, suicide.

Thank you again for your time and consideration. Please recognize alopecia areata as a disease area to be studied. Thank you.

(Applause)

MR. FREY: Thank you very much. Next we have Jessica Lyon from the Morgan Lewis National Brain Tumor Society. And if I could ask Dean Suhr, the next speaker, to make his way up, that would be great. Thanks.

MS. LYON: Hi, thank you. As stated I'm Jessica Lyon. I'm from Morgan Lewis and today I'm here on behalf of the National Brain Tumor Society, the largest non-profit organization in the U.S. dedicated to the brain tumor community.

We applaud the FDA for its work and

request that you consider including brain cancer in the Patient-Focused Drug Development Initiative. Brain tumors and brain cancer are dreaded diseases with no preventive measures and few established risk factors. Brain tumors impact men and women of all ages and tragically are the second leading cause of cancer death in children under 20.

The National Cancer Institute estimates that there are approximately 124,000 patients living with brain cancer. Close to 23,000 Americans will be diagnosed with brain cancer this year and 3,000 of them will be children.

Brain cancer is one of the four most deadly cancers. Glioblastoma, a type of cancerous brain tumor that impacts over 16,000 of those diagnosed with a brain tumor, has a dismal 5-year relative survival rate of 4.7 percent.

Brain cancer fits the criteria set out by the FDA for inclusion in the initiative

as follows. Brain cancer is a chronic disease that unlike many cancers, is not only severe in terms of its physical health, but can also have a devastating impact on one's sense of self, including how one thinks, functions and feels. Survivors, especially children, often face permanent changes in their personalities.

Brain cancer reflects a wide range of severity. For some the standard treatment is helping patients live for an extended period of time with dramatic improvement. For others the standard of care only delivers a year of survival after diagnosis.

There are many aspects of brain cancer that are not adequately captured in today's clinical trials. With the focus of industry to produce drugs that only extend survival, patients in the community want therapies that not only extend their survival, but also significantly improve the quality of their life through both cognition and seizures, for example.

Brain cancer patients who are facing short survival times want the ability to work with clinical trial investigators in a more aggressive manner, particularly with dosing regimens. Patients want more freedom to increase doses rapidly while still keeping safety in mind.

The paucity of approved therapies for brain cancer is both tragic and striking. Only four therapies have been approved by the FDA in the past 30 years. For some types of brain cancer there is no therapy that results in survivorship. Radiation and chemotherapy can extend life for 6 months but there are no long-term survivors.

We thank you for your time and request that you include brain cancer in your initiative.

(Applause)

MR. FREY: Thank you very much. We have Dean Suhr from the MLD Foundation. If the next speaker would make her way up, too.

Thanks.

MR. SUHR: Yes, good morning, Dean Suhr. I'm out from Portland, Oregon. I'm pleased to have this opportunity to come here to the east coast and to speak to you all.

I will reserve most of my comments for written comments because 2 minutes is not much time. But I'm here representing metachromatic leukodystrophy, a rare neurometabolic condition that affects predominantly young children. We're about 1 in 40,000 live births, about 200 population in the U.S. So this is an ultra rare disease.

And while I would love to see MLD as one of the diseases on this panel, I think the more important thing is that the issues surrounding neurometabolic diseases and particularly rare diseases be considered.

We have explicit problems with crossing the blood-brain barrier. We don't have biomarkers and good endpoints, and a lot of that has to do with the patient population

size. And again, if it's not MLD then I'm certainly comfortable with something that's related to that.

We have a sibling survival issue, which means that with delayed diagnosis and not enough smarts and awareness of disease, it ends up being the younger siblings that potentially have access to therapy of which there really isn't a good one for MLD. They're using bone marrow transplants and stem cell transplants with limited effect.

The irony in some of this, and I think the opportunity for us with the FDA is that of the two ongoing clinical trials, the gene therapy and an enzyme replacement therapy trial, as well as soon to be an additional gene therapy trial, are all in Europe. That doesn't help the U.S. population and it is also indicative of some of the challenges we have here with FDA versus EMA and those sorts of things.

The program goals in Section 9 in

C, D, and E were biomarkers, patient-reported outcomes and advancement of the development of drugs for rare disease. Rare disease affects 1 in 10 Americans and particularly this neurometabolic challenge of getting across the blood-brain barrier is something I'd like to see addressed.

So, the rest of my comments I'll send in written form. Thank you.

MR. FREY: Thank you very much.

(Applause)

MR. FREY: Tracy VanHoutan?

MR. VAN HOUTON: Yes. Good morning, my name is Tracy VanHouton and two of my three children are affected by Batten disease.

Batten disease is a progressive neurological disease that has taken my children's ability to walk, talk and eat. It has taken their ability to see the world around them, cause them to need 100 percent care and will likely take their lives by age 10. My son

Noah is currently 8 and a half and my daughter Laine is 6 and a half.

I'm founder of the Noah's Hope Research Fund and vice president of the Batten Disease Support and Research Association. And I'm here today to recommend adding lysosomal storage disorders with neurological manifestations to the list of disease area focus.

Like Dean mentioned, I would like to see my disease specifically added to the list but I think a group that more broadly encompasses this group of neurological disorders would be of great benefit.

These diseases fit the criteria requested for additional disease area selection and they are all poised for near-term success. Curiously, I noted that all the disease areas in the preliminary list have approved treatments. Sadly, for this group of neuro-associated disorders that I am recommending, there is not a single approved

treatment for the neurological manifestations.

These neuro-LSDs including over 45 diseases. Over 40 of these affect children and they are universally fatal.

Batten disease is a chronic specific pediatric disease of known genetic origin resulting in devastating neuronal loss, heart disease and many other symptoms. Investing in development of drugs that focus on these mechanisms and pathogenesis would benefit many of these diseases.

Batten disease is chronic, specific, has a devastating effect on the functions of their daily lives. Children begin their lives normally and slowly begin to regress as they gradually lose all mental and physical abilities.

A previous lack of natural histories, high-resolution endpoints and biomarkers resulted in aspects of this disease not previously being captured in clinical trials. Last week we actually initiated a

mechanism by which to capture these.

Batten disease has a severe impact on pediatric subpopulation. As I noted earlier it was a gradual loss of all mental and physical abilities. And while Batten disease may not represent a broad range in terms of the size of the affected population it is the most common inherited pediatric neurodegenerative disease in the world.

I'll reserve the rest of my comments for written. Thank you very much for the committee's time.

MR. FREY: Thank you.

(Applause)

MR. FREY: Next we have Pam Duquette from NephCure. I apologize if I mispronounce names.

MS. DUQUETTE: No, you got it. Hi, my name is Pam Duquette and I am here on behalf of the NephCure Foundation. The NephCure Foundation is committed to supporting research seeking the cause, treatment and ultimately the

cure of a debilitating kidney disease called focal segmental glomerulosclerosis, or FSGS for short.

We hope that you select primary glomerular disease as one of the disease areas of focus for future public meetings held as part of your Patient-Focused Drug Development Initiative.

My daughter Lindsay standing here beside me suffers from FSGS which is an aggressive primary glomerular disease. FSGS causes scarring of the filtering system of the kidneys, ultimately leading to loss of one's kidneys and death unless the patient is treated with dialysis or a kidney transplant. There is no cure for FSGS and only 25 percent of FSGS patients are responsive to current drug therapies, therapies that are presently limited to harmful steroids and other dangerous drugs that are difficult for patients to endure and can result in permanent bodily damage.

In children, use of high-dose

steroids severely retards growth and development. This is believed to be an autoimmune-based disease.

Lindsay was diagnosed at age 2 and has since experienced 172 hospitalizations including 1 that lasted 76 days, 502 doctor visits, over 4,000 hours on dialysis and 17,000 doses of medications, many very toxic with terrible side effects.

Over the past 8 years she was often in horrific pain and missed all of her first grade and third grade. Her treatment included steroid regimen which stunted her growth and resulted in lumbar bone compression and ultimately she was in a wheelchair and using a walker for several months.

Despite the harsh therapies she endured, we were unable to save Lindsay's kidneys which were removed when she was in her third grade. During the past year she's undergone 14 dialyses, 14 hours a day, and on June 4th of this year Lindsay received a kidney

from her father. We made the decision understanding the risk that FSGS has a 30 to 40 percent chance of recurrence which is petrifying and it leaves us truly every day looking at her urine, seeing if it's going to come back.

The surgery has been successful so far though, and she is currently a fifth grader. Lindsay named her new kidney Raven for her favorite football team and one of Lindsay's concerns was if she was now going to crave wine since she had her dad's kidney. But luckily that hasn't happened and she does still love her ice cream.

Unfortunately transplanted kidneys do have a short life of approximately 10 years and then Lindsay will need another kidney transplant. Regardless, she will take anti-rejection and other medications for the rest of her life.

Primary glomerular disease is an ideal candidate for this initiative given the

outlying disease selection criteria. Primary glomerular disease is a group of chronic diseases that impacts daily living. These diseases impact identifiable subpopulations. They often present in children and are more common in people of African ancestry.

Furthermore, there are no proven FDA-approved therapies for FSGS. And often, the current treatments are often too ineffective.

Finally, this disease group is beginning to attract pharmaceutical interest as recent advancements in research have contributed to our understanding of the causes and mechanisms of these diseases. Dedicating a patient-focused drug development public meeting on primary glomerular disease would be a natural extension of the existing research opportunities, and would contribute to the much-needed therapy development in a manner that best serves the patients.

Thank you again for this

opportunity.

(Applause)

MR. FREY: Thank you. Erika Sward is next.

MS. SWARD: Good morning, my name is Erika Sward and I'm the assistant vice president for national advocacy at the American Lung Association. The American Lung Association is the oldest voluntary health organization and the leading organization working to save lives by improving lung health and preventing lung disease through education, advocacy and research.

The Lung Association wishes to commend the Food and Drug Administration for its proactivity and engagement of the patient community through this initiative and for its commitment to develop treatments and cures for diseases.

The Lung Association will submit more detailed comments next week but I did want to highlight three items. Number one, we were

very pleased to see lung cancer be included on this list.

Number two, we would encourage FDA to consider categorizing diseases that fit together scientifically. For example, while alpha-1 antitrypsin deficiency which contributes to emphysema was proposed on your list of 20 we would recommend that it be included as a subcategory within COPD.

Finally, the Lung Association believes interstitial lung disease, which includes pulmonary fibrosis and sarcoidosis, also very much meet the criteria outlined in the Federal Register Notice, especially since treatments are limited and there are no cures.

Regardless of the 20 diseases ultimately settled on, the Lung Association urges FDA to continue this very important process of engaging the patient community in all aspects of your work. We see this as the start of a very important discussion that we hope extends beyond the specific process.

And finally, one thing to highlight what was mentioned this morning about interest from patient perspectives as opposed to just patient advocacy perspectives. Patient advocacy groups are very familiar with regulations.gov as a way to submit comments to stakeholders. It's a very scary process for people who are unfamiliar with it. We would highly recommend that FDA create an email address so that patients can submit comments directly to you all that be automatically added to the docket. This is something that other agencies including EPA and Interior do and we believe it would be very ripe for having direct patient feedback as part of this process. Thank you.

(Applause)

MR. FREY: Thank you. Next we have Mary Collet.

MS. COLLET: Thank you very much. My name is Mary Catherine Collet. I'm from Indianapolis, Indiana and thank you for the

opportunity to comment today.

We lost mom to ALS over 15 years ago. I know that the FDA does not need an ALS impact statement. You get it and we are grateful for that. You also know about the ticking clock that ALS patients hear. It's fast and relentless. Those patients with their terrible ticking clocks can be a special asset to the FDA in patient-focused drug development discussions.

Whether you discuss risks or endpoints or measures directly with people with ALS that ticking clock is always on the table. That can raise your game just as speed training raises the skills of a world class athlete.

People with ALS ask very good questions. They challenge us all, to borrow a term from Apple, to think different. Some may talk of the frustrations of inconsistent FVC measurements. Some may speak of those last times, dates that the use to index their progression. The last time one could turn the

key in the door lock. The last time one could button a button or blow out the birthday candles.

Some may question today's gold standard, a functional rating scale that buries possible good outcomes among the bad. Some may ask if you are sitting on top of an untapped gold mine of possible control data if only they were gathered at clinic visits. Just the FDA, ALS patients and the ticking clock in the room, without the background noise of the rest of us stakeholders.

Please consider the value that they will add to your insights. Please include their speed training as just a small part of your patient-focused drug development discussions.

I leave you with a quote from Mom. "If you can't cure me, then at least learn from me." Thank you.

(Applause)

MR. FREY: Thank you very much. We have Marcy Povitsky.

MS. POVITSKY: Thank you for the

opportunity to provide public comments today. My name is Marcy Povitsky and I have dystonia. I am here on behalf of the Dystonia Medical Research Foundation to advocate that you include dystonia as one of the disease areas of focus within the Patient-Focused Drug Development Initiative.

Dystonia is a rare, chronic, neurological movement disorder that causes muscles to spasm and contract involuntarily, forcing the body into uncomfortable positions. Symptoms can vary in frequency, intensity, disability and pain and can be generalized, affecting the whole body or focal, affecting specific muscle groups such as eyelids, neck or legs.

Dystonia has a variety of causes, including genetics, head trauma and certain medications. There is currently no cure and only limited treatments including medications, Botox injections and brain surgery.

I was diagnosed with early onset

progressive generalized dystonia in 2001 at the age of 19. Although I have dystonia in my whole body I was most affected by the spasms in my neck and hand. My hand affects my writing which made schooling difficult. Luckily by using a computer I was able to successfully complete both an undergraduate and a master's degree.

My neck spasms were more difficult to deal with. I was unable to hold my head upright and often held it up with my hand. This created an unusual posture which caused neck and back pain and made walking difficult.

Medications did not help so I began receiving regular Botox injections with moderate success. In 2010 after the Botox began to lose its effectiveness, I underwent deep brain stimulation. This device has provided a significant amount of relief, although my non-rechargeable battery does need to be replaced, requiring surgery about every 2 years.

As you can see dystonia falls well within the criteria that the Patient-Focused

Drug Development Initiative is looking for. Dystonia is a chronic disease that affects functioning and activities of daily living. It can affect a patient's ability to move, see and/or speak, often limiting work and social opportunities. Dystonia reflects a range of severity from focal to generalized, and can affect anyone at any age. Dystonia is also presently incurable and current treatments are limited, and can range in effectiveness depending on the patient.

The Dystonia Medical Research Foundation, a non-profit organization dedicated to advancing research and awareness in the entire dystonia community, recognizes the important work of the FDA, and applauds the FDA for taking the first steps to establish the Patient-Focused Drug Development Initiative. We strongly urge the FDA to include dystonia as a disease area of focus in this initiative and hope to work with you to cultivate a comprehensive understanding of the issues

facing patients with dystonia. Thank you.

(Applause)

MR. FREY: Thank you. Anita Roach is next.

MS. ROACH: Thank you for the opportunity to provide public comments today. My name is Anita Roach and I am here on behalf of the Interstitial Cystitis Association, or ICA. Founded in 1984, the ICA is a non-profit organization dedicated to improving the lives of those affected by IC. We are pleased that interstitial cystitis has been nominated for the list of potential disease areas in the Patient-Focused Drug Development Initiative, and we urge the FDA to include IC in the final list.

IC is a condition that consists of recurring pelvic pain, pressure or discomfort in the bladder and pelvic region. It is often associated with urinary frequency and urgency. The condition may also be called painful bladder syndrome or bladder pain syndrome.

It is estimated that as many as 12 million Americans have IC symptoms. The effects of IC are pervasive, damaging work life, psychological well-being, personal relationships and general health. The impact of IC on quality of life is severe.

IC is a disease that falls within the criteria for the Patient-Focused Drug Development Initiative because IC is a chronic disease that affects functioning and activities of daily living. Patients with IC experience urinary frequency and urgency which can impact sleep and other daily activities. The pain of IC can also be -- can cause disability in all areas of a patient's life.

IC reflects a range of severity. IC symptoms differ from person to person and may even vary in the same individual. IC symptoms significantly impact women although the disease also affects men. IC also has a broad range in terms of size of the affected population. Three to eight million women in the United States

may have IC and approximately 1 to 4 million men in the United States have IC.

IC has no cure and none of the therapies tried and used in IC are effective within the total patient population. And also IC has no cure and none of the therapies used in IC are effective.

Thank you for the opportunity to provide public comments today. The ICA strongly encourages the FDA to include IC as one of the selected diseases in this initiative.

(Applause)

MR. FREY: Thank you. Colleen Brunetti?

MS. BRUNETTI: Hello and thank you for having me here today. Before I begin I would like to extend my sincerest thanks to the FDA for undertaking this tremendously important initiative.

My name is Colleen Brunetti and I am a pulmonary hypertension patient. I was diagnosed at the age of 28. I went from planning

a life to worrying that I might not see my baby boy enter kindergarten. Well, that baby boy entered first grade this fall and I was there, and with the help of the Pulmonary Hypertension Association I've learned a lot since those first scary months.

When you get a diagnosis of pulmonary hypertension, or PH for short, your life changes. For some patients, it means a sudden stop of activities once enjoyed because you quickly find you no longer have the breath or endurance to sustain them. For other patients, it is finding the answer they were seeking after too long of searching for an explanation for their symptoms. For me, I also found out I not only had PH, but an autoimmune disease as well, and that's a common scenario with PH.

Because PH is often misdiagnosed, many who finally do get a diagnosis are already in advanced stages with quality of life severely impacted. Medications can help, but often with

severe side effects. The only cure remains a lung and also sometimes heart transplant.

While medications can mitigate symptoms of PH and slow disease progression, and that could be dramatic or minor or temporary depending on the patient. Even when therapy is successful PH is still PH. It's still progressive and the ultimate treatments are still extreme.

The Pulmonary Hypertension Association has blazed a trail of research, education and support, patients, doctors, caregivers, allied health professionals, volunteers, all coming together to put hope in action and to spur us forward until we do indeed reach a cure.

Please select pulmonary arterial hypertension and organ transplantation as disease areas for the initial 5-year pilot program of the Patient-Focused Drug Development Initiative. PHA and the PH community are dedicated to working with FDA in a meaningful

and constructive way to ensure this pilot program is a success.

It is not only our goal to see that patient experience better informs regulatory decision-making for PH, but that this effort grows into a sustained campaign of close collaboration between FDA and all patient communities which continuously improves the system for reviewing and approving innovative therapies. Thank you.

(Applause)

MR. FREY: Thank you. Terry Robert?

MS. ROBERT: Good morning. My name is Terry Robert. I'm here on behalf of the patients represented by the Alliance for Headache Disorders Advocacy and the American Migraine and Headache Association. I'm also a migraine patient myself and have four grandchildren with migraine.

The WHO in their assessment statement has said that there are more lost years

of healthy life in the U.S. lost annually to migraine than epilepsy, MS, ovarian cancer and tuberculosis combined. They have also stated in that assessment that a severe migraine attack is as debilitating as quadriplegia.

There are 37 million migraineurs in the United States. It impacts women disproportionately at a ratio of 3 to 1. Migraine does not bias itself by age. My granddaughter had her first one at 2 and a half when she was too young to tell us what was wrong. It also continues sometimes into old age.

Migraine also presents other risk factors, such as increasing our risk for stroke and cardiovascular disease. There is not a single medication on the market that was developed originally for the prevention and management of migraine, not one. All the drugs we have are hand-me-downs from other conditions.

When it comes to the medications for aborting a migraine attack in progress, the triptans and ergotamines, they are each and

every one of them contraindicated if you have a history of or risk factors for stroke or heart disease. Not a good situation.

We will be submitting further comments in writing. I want to thank you for this program and for this opportunity to speak here and to ask you to consider adding migraine disease and other headache disorders into your considered list. Thank you.

(Applause)

MR. FREY: Thank you. Carol Pasinkoff.

MS. PASINKOFF: First I would like to thank the FDA for this opportunity to speak and enlighten you about what gastroparesis is. My name is Carol Pasinkoff. I live in Bayside, New York, and I've had gastroparesis since 2004.

I am an FDA patient rep for gastroparesis as well as a board member and patient advocate for an organization called Gastroparesis Patient Association for Cures and Treatments, better known as G-PACT. G-PACT is

a non-profit organization trying to raise awareness for gastroparesis, chronic and pseudo obstruction and colonic inertia.

What is gastroparesis? Gastroparesis, or as it's often referred to as GP, literally means paralyzed stomach. It is one of the most severe and complicated gastric motility disorders to diagnose. In GP the body loses the ability to digest food normally. The stomach does not contract as well as it should if at all. This results in delayed gastric emptying of food and liquid into the small bowel. Often food will sit in the stomach for several days. It is not uncommon for patients to vomit undigested food eaten many days earlier.

The symptoms include nausea, vomiting, bloating, pain, belching, feeling full after a few bites, weight loss, malnutrition, dehydration and fatigue. Gastroparesis can be caused by diabetes, post-surgical, post-viral, from autoimmune disorders or if there no known cause, it is

called idiopathic, which is the type of GP I have.

According to the National Institute of Health there are 5 million people in the U.S. that have gastroparesis and unfortunately there are very few treatment options available and they are not very effective.

Gastroparesis is very debilitating. It is life-altering. It is very hard to work feeling so sick and weak. It causes many of us to lose our jobs, friends, medical coverage. It is very hard to obtain disability benefits with a GP diagnosis which in turn causes extreme financial hardship on many. There are frequent hospitalizations for hydration, nourishment, electrolytes and pain relief.

As well as malnutrition, many of us suffer from extreme tooth decay due to the acid of vomiting and regurgitation. We periodically need IV infusions of iron, potassium and other vitamins. Our bone health suffers and many of us have severe osteoporosis. We take many

medications to help with dealing with the symptoms but there is no cure. I personally take over 30 pills a day just to function and there are some days the nausea is so bad that no combination of medication helps.

People with digestive tract paralysis have problems living a normal life. It directly impacts daily living as you never know how you're going to feel at any moment or what will trigger you. The nausea is unrelenting. Think of the worst stomach flu you've ever had and imagine feeling that way every single day of your life. There are some days that I can't even get out of bed.

Our social lives are affected. Everything in life revolves around food. People get together to celebrate life events and food is always involved, or people get together for dinner, barbecues, coffee and cake, et cetera. Gastroparesis is very isolating and depressing.

There are different degrees of

severity of gastroparesis. Some people can eat following a very, very strict diet. Others survive by living on liquid diets. Many of us are either intravenously fed with TPN which has many problems associated with it such as line infections and liver failure. I almost died several times from severe line infections and I've had 16 different lines put in during a 2-year period. Now I am tube-fed as so many of us are and there are others that have had multi-organ transplants as our founder of G-PACT, Carissa Haston, did.

This past month we lost seven people due to malnutrition and line infections, and for this and the fact that there is absolutely no cure for us we ask the FDA to consider gastroparesis as one of your disease groups. Thank you.

(Applause)

MR. FREY: Thank you. Tom Murphy.

MR. MURPHY: Good morning. My name's Tom Murphy. I was diagnosed with ALS

in December 2010 so I'm about halfway into sort of the death sentence if you will. And I wanted to talk a little bit about this as an opportunity for ALS.

I feel that we in the ALS community have an unprecedented and maybe historic opportunity with this initiative. For the first time in over 100 years we can actually see some real progress with respect to several treatments that are currently in FDA-sanctioned clinical trials and have a realistic chance to slow disease progression, improve quality of life and/or extend our lives.

So there's three drugs in that category and two stem cell treatments right now. I won't name them all but -- so we're in a situation where none of these treatments have been formally approved or conditionally approved for marketing yet by the FDA and there's also been no movement in the area of expanded access or compassionate use in these areas. But if there was ever a critical point in time

for all ALS patients to have a say in the risk-benefit decision process it is right now when several treatments should be being considered for approval, conditional approval and/or expanded access.

I feel and so do a significant percentage of ALS patients that ALS could greatly benefit from a more systemic and expansive approach to obtaining the patient perspective on disease severity or unmet medical need, and more importantly, could become a terrific example for the success or non-success of this PDUFA V initiative. I won't call it a pilot. I'll call it an opportunity.

And given the confluence of events, several decision events that are probably going to happen in the next 6 to 18 months with five treatments, what a tremendous time to start to really have something like this in place for ALS patients.

Finally, I'd like to recommend that these sessions and processes designed to create

this more expansive approach really needs to include not only the patient and the FDA but also the pharmaceutical companies and the disease experts and doctors. These are all critical players and stakeholders in this process and I think we all know that if they don't all work together it's, you know, individual people aren't going to make it happen.

And I have one other thing that I think is important to talk about in terms of opportunity. This community, the ALS community, seems to have a very interesting Patients Like Me where several thousand of us interact and talk to each other every day and talk about our disease and what's happening.

And this would be probably another opportunity for the FDA to look into information technology, business intelligence and a way to get a really broad patient perspective in a very specific area. So that might be a good thing. So, thank you.

(Applause)

MR. FREY: Thank you.

MR. MASTROFRANCESCO: Good morning. I'm not an advocate, I don't get paid to come here. I came here on my own accord. I was an aircraft mechanic but now I'm a patient. And I don't want to bore everybody with all the people here with ALS but I happen to be one of them. I was diagnosed last year.

I do want to make one comment on the identifiable subpopulation. ALS affects generally men in middle age which is going to include men with families including myself. I've got three children and many of them are still underage and are going to require an awful lot of help from somebody who is not going to be capable of doing so.

I am willing to talk with you guys about what I'm going through. I'm willing to experiment on my own body and I have due to lack of other potential therapies out there. I've taken many risks but I've also tried to seek

the counsel of the best doctors in the country and I've been to them.

I have found that the therapies that are offered to me are either none or inconsistent. I've been told okay, yes, try that, get on that, and then I go to the next doctor and they say oh, don't do that, that could make you worse. These are the kind of things that you guys should hear about from people like me at this time so that you can find out from me or from my other colleagues and patients that have been on trials and have found some efficacy in what they were getting, and then they were -- the drugs have been taken from them. And then they get worse.

And we are very desperate for somebody to listen to us right now. The only other option, you know, people have mentioned the word suicide and I try not to but it's a very, very difficult place to be in our situation. And when we look at the list of the types of things that you guys want to focus on,

I don't want to make anybody upset in this room, but some of those things I'd be happy to have the doctor walk out of the room and say well, Mark, we've just discovered you've got this instead. We'd have a party.

I really think that you guys have overlooked the opportunity to get people with Lou Gehrig's disease in here and get their perspective. I hear it from everybody. You get on the internet, we want to tell you what's going on, we just need somebody to listen to us. Thank you.

(Applause)

MR. FREY: Thank you. Mary Dimmock.

MS. DIMMOCK: Thank you. My name is Mary Dimmock and I'm a member of an alliance of patient organizations and patient advocates representing patients with chronic fatigue syndrome also known as myalgic encephalomyelitis or ME/CFS.

The popular misconception is that

CFS is chronic tiredness due to de-conditioning, depression or poor diet. That's what I thought until my energetic, smart, adventuresome 23-year-old son was struck down by CFS after contracting giardia while backpacking across Asia.

Overnight he went from academic excellence and scaling mountains to being unable to work, seldom able to leave the house and too often unable to do more than lay on his side in a dark room in constant pain.

He is not alone. One million Americans of all ages, races and socioeconomic groups and 17 million people worldwide have been struck down by this complex multi-system disease that causes significant immune, neuroendocrine, cardiovascular, autonomic and energy-producing impairments. As a result patients suffer devastating functional impairments that result from profound exhaustion, unrefreshing sleep, joint and muscle pain and cognitive problems that include difficulty thinking, slower

processing speed and impairment of memory.

These symptoms are exacerbated by even very minimal mental or physical activity and can result in a relapse that lasts days, or weeks. The CDC has said that CFS can be as disabling as multiple sclerosis, lupus, rheumatoid arthritis, heart disease, end stage renal disease and other similar chronic conditions. Patients can be sick for decades. In fact, many have been sick since the outbreaks in the mid-eighties.

Twenty-five percent of patients are bed-bound, house-bound or wheelchair-bound. Ten percent of patients are pediatric, some as young as 5. The inability to attend school, play with friends or even participate in family activities during their developmental years has a particularly harsh and lifelong effect on these children. Overall, recovery is rare and one study found that patients are more likely to die prematurely from cancer, heart disease, or suicide. And yet today there are no

treatments for CFS that are capable of even minimally improving patient functionality or changing the long-term outcomes of this disease.

There is only one disease-modifying drug being progressed through the FDA process. A lack of agreement on definition, endpoints and outcomes has impeded significant investment from the pharmaceutical industry. The drugs that are used are used only for very limited relief of specific symptoms like pain but have little impact on the overall level of functioning.

The resultant reality for my son and for many patients is that they will spend the rest of their lives in pain, disability and isolation, functionally so limited that they are unable to work, care for their family or even sometimes take care of themselves.

Please include CFS in the Patient-Focused Drug Development Initiative and take a close look at the severity of this disease, the dramatic loss of functionality that

these patients experience and the complete lack of approved treatments. Please look at how 1 million Americans view the benefit-risk of a drug that would give them back even a portion of their lives. Thank you.

(Applause)

MR. FREY: Thank you. Joe Landson.

MR. LANDSON: Good morning, I'm Joe Landson. I've had chronic fatigue syndrome for 8 years.

I'd like to thank the FDA for the recent teleconference it held to interact with other CFS patients and I was very encouraged by it. I was troubled by something I heard during the call though, looking at outcome measures by way of measuring subtle differences in fatigue. I think this has been pursued already and not very successfully. We might want to stick more towards looking at immune markers that we have or other biomarkers that we may discover down the road.

The word "subtle" bothered me

because I don't feel I have a subtle illness, not when I'm occasionally bedridden and not when it'll take me several days or perhaps up to a week to recover from attending this meeting.

If it's just a difference of subtle fatigue it's probably not worth adding CFS to your list. However, if it's the devastating illness that has kept me from working full-time and sometimes at all since 2006 it might be worth putting up there. Thank you very much.

(Applause)

MR. FREY: Thank you. Annie Kennedy.

MS. KENNEDY: Good morning. I'm Annie Kennedy and I'm with the Muscular Dystrophy Association. We represent more than 40 neuromuscular diseases which includes the muscular dystrophies, spinal muscular atrophy, ALS, Charcot-Marie-Tooth disease, Friedreich's ataxia, the mitochondrial disorders, congenital myopathies and many others.

Thank you for providing this vital

platform today for interaction and dialogue. We're very appreciative of this.

We support an approach which was mentioned earlier today of identifying disease areas and establishing meetings based on clusters of diseases that have similar profiles in terms of the criteria that you proposed.

From this approach we ask that you consider a meeting focused on neuromuscular diseases within your criteria. Without going through your entire means test, our community has found that this approach of considering these disorders together when appropriate in clinical and research design is a force multiplier.

Many of our neuromuscular diseases share disease course and age of onset. They are severe, progressive diseases that have a profound impact on daily living. Many have devastating cardiac and pulmonary implications, all impact physical mobility.

While our clinical communities are

very well organized and our research is robust we have significant unmet medical needs and all but one of our neuromuscular diseases have no life-altering treatments to date.

A meeting of this neuromuscular disease cross-section would allow us to focus on commonalities within our diseases such as burden of disease, clinical outcome measures for communities who are not currently eligible for our clinical trials, increased understanding of clinical effect of therapies under development, clinical trial design and risk-benefit analysis.

Additionally many of the clinical and research experts within our disease areas are experts in more than one of the rare diseases within our community. For all of these reasons we strongly encourage a cluster approach of meeting selection and ask that neuromuscular disease be among those that you prioritize on this list.

Again, we thank you very much for

your effort not just today but your ongoing commitment to our communities. Thank you.

(Applause)

MR. FREY: Thank you. Julie Flygare.

MS. FLYGARE: Hi, I'm Julie Flygare here on behalf of patients with narcolepsy. I'd like to thank you so much for this opportunity and urge the FDA to please select narcolepsy as one of the 20 disease areas for this important effort.

Narcolepsy is a neurological autoimmune disorder affecting 1 in every 2,000 people in America. Extremely under-diagnosed, therefore you don't hear much about it but it really does affect about 200,000 people it's estimated.

The effect upon quality of life is compared to epilepsy and Parkinson's disease. It's a very complex disorder in which patients don't all experience the major symptoms. Some affect some of them, some are affected by all

the symptoms. I'm affected by all four of the major symptoms, excessive daytime sleepiness which is comparable to how a person without narcolepsy would feel after they had not slept in 72 hours. I experience that amount of fatigue two or three times a day.

Cataplexy is another major symptom I'd like to highlight in which I experience full muscle paralysis when I have an emotion. What that feels like is a little bit like being conscious in a paralyzed body. I fall to the ground and I can hear everything around me but I cannot move a finger, a toe, nothing. Everything is paralyzed and may look like I'm asleep because your eyelids are muscles, your jaw is a muscle, everything.

This obviously can have a huge effect on people's education, their employment and their personal lives. We have no cure and despite the best treatments people's lives are still very much affected. There's no treatment to actually affect some of the major symptoms

of narcolepsy and certainly no treatment that affects all of them.

Once I was diagnosed I assumed I would take medication and be better, and I was very surprised to end up in the ER on the third day of that and currently take medication twice a day and twice a night. Despite looking healthy on the outside my life became a living nightmare. I was in law school at the time and I was spending most of my time in the restroom nauseated, gagging, crying.

And it's really a 24-hour job to have narcolepsy. It affects every decision I make, when I can eat, drink, sleep, drive, walk, exercise, everything. This is what goes through my head.

I believe the FDA will gain invaluable perspective by taking the narcolepsy patient perspective into consideration. Thank you very much.

(Applause)

MR. FREY: Thank you. Karen

Kramer.

MS. KRAMER: Good morning. My name is Karen Kramer and I'm here on behalf of FORCE and other organizations which represent millions of Americans living with hereditary cancer syndromes including those with BRCA mutations, Fanconi anemia, AT, Lynch, Cowden and Li-Fraumeni syndromes.

Our communities face cancer risks up to 50 times greater than the general population. Hereditary cancer syndromes are known to increase the risk for breast, ovarian, endometrial, colon, pancreatic, prostate and many other cancers.

Hereditary cancer syndromes offer unique opportunities for exploring the known gene defects and associated genes to develop population-specific treatments and preventions. However, they also offer distinct challenges, including the fact that hereditary cancers are rare and consist of a smaller subset of the larger cancer cohort. As such there are

fewer financial incentives for pharmaceutical companies to target these cancers versus the larger disease populations.

And tests to identify and define members of hereditary cancer populations create their own challenges to therapeutic development because they are expensive, lack FDA approval, or simply aren't utilized.

Nevertheless, it is important to develop new preventive and therapeutic agents for those with inherited cancer because of their unique challenges, challenges such as the lifetime risk for familial cancer is significantly higher and cancers often strike younger and are more aggressive than sporadic cancers. This may lead to a different risk-benefit ratio for prevention and treatment for those than sporadic cancers.

The genes and pathways associated with these cancers are frequently known, lending the opportunity to target vulnerabilities that may not exist for sporadic cancers. Hereditary

gene mutations are sometimes associated with different risks and benefits for therapeutic agents compared with published standard of care for sporadic cancers.

And hereditary cancer syndromes provide a scientifically unique opportunity to develop targeted therapies, paving the way for next-generation diagnostics and therapies that will be applicable to the broader cancer community.

PARP inhibitor research and the challenges in developing this class of drugs for those with BRCA mutations offers an example of why it is crucial for hereditary cancers to be considered as a unique condition for patient-focused drug development. These identifiable subpopulations within the broader cancer community are profoundly impacted by their high risk for multiple cancers, cancers that often strike younger and are more aggressive than sporadic cancer. Few if any clinical trials appropriately address the needs

of this population and there are currently no therapies available that target the distinctive traits of these syndromes.

We urge the FDA to add hereditary cancer syndromes to the list of disease priorities in the Patient-Focused Drug Development Initiative. The hereditary cancer community bears a very heavy cancer burden and together we can remedy this injustice while optimizing the promise of personalized medicine. Thank you.

(Applause)

MR. FREY: Thank you. Jamie Troil.

MS. TROIL: Hello, my name is Jamie Troil Goldfarb. I have stage IV melanoma and I also represent the Melanoma International Foundation which in turn represents thousands of patients globally.

Although responsible for a death every hour in the United States, most people do not understand the deadly skin cancer that is melanoma. They don't take steps to prevent

it, they don't know how to detect it and they have no understanding of the complex treatments that it requires.

Outside of the standard chemotherapy, radiation and surgery we have only two main standards of care, immunotherapies, both of which offer very low response rates and even lower cure rates. The discovery of targeted therapies and immunotherapies are making melanoma a chronic disease as people are living longer, but stage IV melanoma carries only a 15 percent 5-year survival rate.

Someone dies from melanoma every hour and an estimated 44,250 new cases of invasive melanoma in men and 32,000 in women will be diagnosed in the United States alone in 2012.

Melanoma skin cancer is the most underfunded of all cancers by federal and private agencies. Although early detection makes it highly curable it's the least screened-for cancer.

Although people are living longer thanks to some recent strides in research, the vast majority cannot be cured. People are moving from one treatment to the next buying as much time as they possibly can before they exhaust their treatment options.

The treatments are physically demanding and the emotional toll of living with a disease that is most likely fatal is indescribable. The majority of patients undergo numerous surgeries and submit to being burned through radiation, poisoned through chemotherapy before ever being told about the immunotherapy standards of care by which time they're often ineligible to receive them because of their toxic side effects.

The difference in severity between stages like any cancer is vast. Treatment depending on stage ranges from simple removal at your dermatologist's office to extremely difficult inpatient immunotherapy treatments that carry horrendous side effects from extreme

nausea, vomiting and diarrhea, to full-body skin rashes and peeling, to hallucinations and night terrors.

For stage III melanoma, the only approved adjunct therapy is chemotherapy which is in itself highly controversial as it does not show reduced progression. And those two standards of care for stage IV melanoma yield 15 percent response rates at the most with only a 5 percent cure rate in one of them.

As far as clinical trials, new therapies for melanoma are being discovered quickly and the research pipeline does hold a number of promising treatments. As immunotherapies they are highly complex, highly personalized and extremely expensive. They represent costs in the hundreds of thousands of dollars per patient for the research sites and study sponsors and some of the most promising trials such as the National Cancer Institute's adaptive cell therapies are cost-prohibitive for widespread adoption.

The ideas are there and the knowledge is there, we just need more resources to facilitate bringing these investigational treatments to the general public.

As is with the case of many cancers, clinical trials represent some of the best treatment options for stage IV patients. However, industry statistics show that only 8 percent of oncologists ever talk with their patients about clinical trials which leads to only 5 percent of oncology patients participating in clinical trials.

Melanoma is on the rise in young men and young women specifically. It's the most common killer of young women, more common than breast cancer in women age 29 to 34 and women under the age of 39 have a higher probability of developing melanoma than any other cancer except for breast cancer.

For stage III disease there's little to offer melanoma patients. The only adjunctive therapy approved is interferon which

has not been shown to increase overall survival and has many toxic side effects. Of the approved drugs for stage IV, interleukin-2 and ipilimumab, marketed under Yervoy, offer 15 percent response rates at the most with ipilimumab having no proven cure rates and IL-2 having a cure rate of only 5 percent. There are two more mutation-targeted therapies but they're only possible for 40 percent of patients.

Myself, I have undergone eight surgeries for melanoma and I spent 4 months out of 2012 in in-hospital treatments at the National Cancer Institute. A clinical trial at the National Cancer Institute is saving my life but it was a very radical treatment and I was only the ninth person in the world to ever receive it. It basically involved a full immune system transplant with genetically engineered cells to fight tumor.

So we greatly hope that you keep melanoma on your list. We need treatment

options because we're dying and we're dying quickly. Thank you.

(Applause)

MR. FREY: Thank you. Ron Bartek.

MR. BARTEK: Hello, Ron Bartek. I'm co-founder and president of the Friedreich's Ataxia Research Alliance. I'd like to join my voice with those that have already commended and applauded the Agency for this program today and for your very active and eager implementation of the PDUFA V FDASIA mandate. And not just the selection of 20 disease areas that will improve the education of the review divisions in terms of these diseases but also the other communication systems that you either already had in place or are going to implement even more aggressively following this legislation.

And added to that, the meetings that many of the advocates in this room have already participated in in helping that education process, the milestone meetings, the pre-IND

meetings and so forth. These are all going to be pulled together very assertively by this kind of operation and we appreciate and applaud that.

Also would like to join in the voices you've already heard today and probably will hear additional voices to this effect, that as you select in this very important Patient-Focused Drug Development Initiative 20 disease areas that you focus not on 20 specific diseases but on 20 disease areas.

That would include diseases that would answer to the same four key factors in almost identical fashion. The same impact on quality of life, the same severity or burden of disease, the same impact on a subpopulation like children or the elderly and the same lack of treatment.

And by doing so we think there's a wonderful opportunity for your review divisions to learn about whole clusters of diseases in the same meeting. And instead of dealing with 20 specific diseases you might deal with 200

diseases and get that much closer as long as they have next to identical or identical in terms of those four key factors.

We recognize too that there's a lot of work to be done by the advocates and the patient groups to assemble those sort of clusters and confirm for you that we believe that our diseases are next to identical in those four key factors and would love to bring them to you. So thank you very much for this opportunity.

MR. FREY: All right, thanks. One note. As you noticed that we're running over time. We have another slide of folks who want to speak but I think what we're going to do is address these during the second comment session.

So I think if we can move to the second panel we will do a switch here. And we'll try as best as we can to make sure everybody has a chance to speak during the second session.

I'd like to introduce Anne Pariser. She's our associate director for rare diseases

in CDER's Office of New Drugs.

DR. PARISER: Thank you, Patrick, and good morning. I'm going to switch gears a little bit and we're going to move to incorporating patient perspectives into drug development into the FDA process. And I was specifically asked to talk about things other than the patient-focused drug development which you've been hearing so much about. And just to put that in a little bit of context I'll also talk a little bit about FDA's role in drug development and try to cover all this in 10 minutes or less so I'm probably going to speak pretty fast.

As Dr. Woodcock mentioned earlier FDA's role in drug development generally starts when you begin the testing of a potential agent in humans. This is towards the second half of drug development. There's usually a lot of work that has gone on up till then and also as Dr. Woodcock mentioned we tend to set the standards for how earlier research is done because we will

be using this and do need quality scientific investigations. And just a little bit of terminology that I'll be talking about. IND is investigational phases, clinical development in humans. And the marketing application comes towards the end of drug development where you've taken all that you know and gathered it together and then submitted it, and if all goes well it becomes an approved commercially available product.

So what is not typically under FDA's oversight is basic scientific research, translational research if it is non-interventional, and pre-clinical research, although this is information that we do use and we do care about very much.

So this is a gross oversimplification, high-level look of drug development. Starting typically here, basic science, laboratory investigations, moving into translational phases. Pre-IND comes right before clinical investigations and then the

marketing and approval process is towards the end.

The time lines are highly variable. This is a very complex process that involves many people to try to bring these through all the way along the process. This is typically where some of the various stakeholders get involved, and FDA you can see gets involved right down here right as you're moving into clinical trials.

NIH is typically involved in the basic scientific research either directly or through their granting. FDA is not a funding organization and also as Dr. Woodcock mentioned we do not perform the research.

Drug developers can actually get involved anywhere along here but typically again towards clinical trials although sometimes they do develop basic science. So I think what should be obvious here is there's a very big translational gap, sometimes referred to as the valley of death.

And recently both FDA and NIH have been trying to step into this space to try to facilitate and build that bridge from the basic scientific developments into clinical trials, some of which I will mention here. FDA tends to call this the critical path of regulatory scientific development and NIH tends to call this translational science.

And also as you've heard, to be approved, a drug has to be shown to be safe and effective, the benefits outweigh the risk and that's what we're discussing here, is this substantial evidence which needs to be clinically meaningful. And what we frequently tell drug developers is, have you talked to the patients. It's the patients who are the people who should be telling us what is clinically meaningful to them.

So this is just to represent the magnitude of the problem. And I think some of you have really heard about this already today. There are an awful lot of diseases, there's

tremendous unmet need and a lot of serious disorders. And thank you to all of you for sharing your personal stories with us today.

And the reality is I spend all my time working on rare diseases. There are about 7,000 different rare diseases. The vast majority do not have any approved therapies or even any research, and that's represented by the part down here beneath the water where you can't see it.

But common diseases as well have unmet medical needs and the way things are going now even common diseases are becoming rare diseases. So we need to really find ways to move as many of these above the water, chip away at this iceberg and try and move things forward as efficiently as we possibly can.

So these were some of the major goals under FDASIA. Now, some of this is not new but some of this is and has come under renewed and more important focus in a number of provisions in FDASIA. And I'm only going to touch on some

of them, but just to focus on the two at the bottom here. There's much more of a focus on regulatory scientific development, that translational phase, benefit-risk and the patient voice in the process. And there are several provisions to include the perspective of patients. And I'm just going to mention just a couple of them.

So some of the major initiatives include serious life-threatening, life-limiting disorders or those with unmet needs. We have something called breakthrough designation for those drugs that appear to have some evidence that they represent meaningful advances, increased emphasis on accelerated approval, rare diseases and again, regulatory science. And all of these bring opportunities for interaction and engagement and development of that regulatory science.

And also under patient interactions of course you've heard about patient-focused drug development but I'll just mention a couple

more. There's also fostering participation in the patient representative program which I'll just say a word or two about, and something called expert consultation.

So, just to echo what has been said several times now. In addition to these 20 meetings this is really intended to inform all drug development. We are trying to develop a framework, a process, learn from experience, run these pilots and really there is considerable emphasis here on learning. And we are trying very much to learn from all of you.

This is just a snapshot of FDA's website for the patient representative program. This is run out of our Office of Special Health Issues. I don't have time to read through it all, but I did provide this on my slide so that you can look this up at your leisure, but this is not a new program. It's been around since 1991. But we're looking to expand this program.

And this specifically is a way of

having patients or patient representatives serve as what's known as special government employees to FDA during advisory committee process but also during drug review process. It does require a lot of paperwork and some time and some training. But this has been something that has been very valuable to us.

This is Tiffany. I put her picture up on the slide. She has served as a patient representative and I personally have worked with her, and I can attest that this was an extremely valuable experience for us in considering drug development. So I would urge you all to take a look at this up on our website and to see if there are opportunities for you to be involved.

I'd also like to mention expert consultation. This is specifically for rare diseases and it's for the purpose of promoting efficiency and information in drug review where FDA is being encouraged to interact with outside experts.

But what I would like to point out,

here is an expert as defined as someone who possesses scientific or medical training, including willingness and ability of individuals with rare disease to participate in clinical trials and assess benefit and risk of therapies. So, that does include patient advocates as experts and consultants. So this again requires things like going through the special government employee process. But this is another opportunity to interact.

So I'd just like to leave you with a couple of key points. There are numerous opportunities for involvement of the patient voice and the patient perspective in drug development, not just these meetings. This is of most value when we can involve you early on in the process and go back over it at different points as more knowledge is gained. And this is extremely informative to both efficient and rigorous scientific development. It is impossible to overstate the importance of this.

We're going to be hearing an example

actually from a patient advocate just right after I finish speaking, but some of the areas that are really important are disease natural history, the endpoint development and the meaningfulness of the interventions and the clinical outcome assessments.

Just as one example this was also mentioned by Dr. Woodcock earlier, but this is not by any means the only example. I hear about these examples every single day. The CF Foundation is just one of the longer-standing organizations. They actually were established in the nineteen fifties. They started their registry in 1960. They have extensive history on this disease.

This has led to many other things, patient care standards, centers of excellence, a research program and what it has resulted in is a very robust pipeline for drug development and efficient drug development. So unfortunately time does not permit more discussion on this but just trying to illustrate

how important this is and how this can be incorporated into the process.

So I'll just leave you with one last thought. My last slide is communication, collaboration, transparency. These are key features in FDASIA and especially increased outreach. You heard from some of the division directors. They've been doing this for a long time but it's something we want to do more of. Public meetings, workshops, interactions with the review division. Collaboration with FDA but not just with us, also with NIH, academia and industry. If we can all get together preferably in public meetings and brainstorm good things tend to really happen. So thank you very much and I'll stop there.

(Applause)

MR. FREY: Thank you very much, Anne. A great segue. We have a patient advocate here to talk about what she has been able to do in advancing drug development in Phelan-McDermid syndrome absent any assistance

from those of us who have to implement patient-focused drug development in FDA. So, I'd like to introduce Megan O'Boyle.

MS. O'BOYLE: Good afternoon and thank you for having me.

(Applause)

MS. O'BOYLE: Wow. As the only patient invited to stand at this end of the podium I have 10 minutes to represent 7,000 rare diseases and countless common diseases. So clearly there's no pressure on me here at all.

In light of this daunting responsibility I would like to speak beyond my experience and my own child's disease. But in fact it is my own child, Shannon, and her disease, Phelan-McDermid syndrome, which for those of you who keep track of acronyms it's PMS. It's an unfortunate acronym.

This is a deletion of the 22nd chromosome 22q13 and it's considered now a genetic cause of autism. We do not know the true population but at this time we have 820

families in the world that belong to our foundation. If everyone with intellectual disabilities or in the autism spectrum were tested we would have tens of thousands, still being a rare disease.

Our children's deletions and mutation sizes vary and their phenotypes vary. One thing we all know is that our children are missing a gene called Shank3 which makes a protein called Shank3. And I can assure you that everybody in this room should thank their lucky stars that they have an intact Shank3.

Like many patients with fragile X, Angelmans, tubular sclerosis, Rett's and other known genetic causes of autism our children have severe intellectual disabilities, low muscle tone, seizures, GI issues, sleep issues, sensory issues and so on. Part of the reason I am here today is to speak on behalf of my non-verbal child who will probably most likely never have communication.

Autism of known genetic cause is a

perfect example of a cluster of diseases that could be presented by the FDA reviewers. I was invited today to explain what our foundation has done to further research in drug development.

For the most part we're just a group of parent volunteers. We don't have a scientific director and we've only had a research committee for 3 years.

So, what has motivated a bunch of parents to do something in 3 years and what have we accomplished? Well, our children have motivated us. And what we've accomplished is like many of you other groups we have sponsored some research symposiums. Of the two that we were able to sponsor one was across different diseases. Our Shank3 gene actually has interaction with -- or degradation with Alzheimer's and schizophrenia, two seemingly unrelated diseases for whom we have a molecular connection.

We're good like this. We're good

at thinking out of the box. We like to be creative and we like to consider others. We've also offered fellowships and other incentives for young investigators. Thanks to our researchers for whom we do not fund we have knockout mice, iPS cells and a comprehensive patient registry and biorepository. This is not too bad for a bunch of volunteer moms.

The research effort that I am most familiar with is the establishment of our registry and biorepository. This is the only registry and by this for technical purposes I'm going to call it a young natural history study. And it's the only one in the world, and the data includes more than 200 data points including the genetic results of all of the patients.

We have 480 families registered in less than 2 years which is a high percentage considering we only know of 800 families worldwide.

You may wonder why a patient advocacy group with very little resources would

take on such a project. Well, this will better define our disease and it will allow us to have as a foundation control of our patients' data which belongs to them. But we can also make it available to researchers around the world as opposed to having a researcher hoard the data in one silo.

We also want to save the researchers and pharmaceutical industry time and money. We are finding and consenting our families. We're collecting their data and their bio-samples. We want to be the best guinea pigs we can be. Ultimately we want to make the FDA review process, once we do get to clinical trials, simply easier.

I recently had the honor of sharing our first year of data with four members of the FDA. I called them and simply asked for their advice and they agreed very generously to look at what we did and let me know if we were on the right track so down the line we would have what they would need.

To my pleasant surprise they were impressed with our efforts and our results. They encouraged us to continue what we are doing and to offer our example to other rare diseases in need of moving their research forward.

I want to thank the FDA for inviting me here today and for all of you for taking the time to listen. We are babes in the woods compared to many of your organizations and I would be remiss if I did not take this opportunity to request that the decision-makers please consider looking at this list to be reviewed as clusters of diseases.

I am offering the services of NORD without their permission, but this is a public meeting and they can't really say no now, to go ahead and organize diseases into clusters so the FDA wouldn't have to.

You know, autism is already on this list, I don't need to make its grade, but looking at genetic causes of autism would do what we've been asked to do. And looking at groups like

this, and there's probably 20 or 30, you can consider severity, impact of quality of life, impact on subpopulation and lack of treatment. They're all going to have similar measures.

We believe that therapies born from research of these rare genetic causes of autism will lead to therapies for the greater population which is now estimated to be 1 in 88 persons. Thank you again for allowing me to be here today and please if your foundation has been successful in some way in forwarding research, please share that with other foundations, as we all need treatments. Thank you.

(Applause)

MR. FREY: Thank you. And we have Jason Lundy from the Critical Path Institute's Patient-Reported Outcomes Consortium.

DR. LUNDY: Thank you. Hello, I'm Jason Lundy from Critical Path Institute in Tucson, Arizona and I'm the assistant director of the Patient-Reported Outcomes Consortium,

PRO for short.

And I realize we only have 5 minutes until we get back to the comment period so I'll keep my remarks brief. But I did just want to talk a little bit about what we do, what we're about, how we incorporate the patient's perspective in things that we're doing and what our ultimate mission and goals are.

C-Path was started in 2005 as a response to the Critical Path Initiative. In short that initiative aims to speed and provide efficiencies to the drug development process. The PRO Consortium specifically was started in late 2008. Our first active year was in 2009. I joined on January 1st in 2010 which I think was a Saturday or Sunday so that gives you kind of an impression of how serious we take the work.

Our goal really is to provide a voice to the patient in determining whether a drug works. That's what I'm passionate about as a scientist. I'm also an IBS patient. My father suffered from MS. So I know what it's like to

experience these types of symptomatic conditions that are quite variable on a daily basis. And that's really what we're all about.

We're currently working in seven disease areas, asthma, IBS, depression, mild cognitive impairment due to Alzheimer's disease, non-small cell lung cancer. We've recently started a functional dyspepsia working group as well as a rheumatoid arthritis working group.

The patients are critical in everything that we do. It's actually the first step in any of the projects that we take on, is to go out and talk to the patients that have the disease that we're looking at and ask them, tell us about a day in your life, tell us about the symptoms that you've experienced and how did those impact your functioning and your quality of life. And from there really that is the basis of developing new endpoints, developing new patient-reported measures and outcomes that can be put into clinical trials

to test whether these drugs work.

And some of you may say well, don't we already have enough PRO endpoints out there, can't we already use them. And to some extent that is the case and there are some good ones that are in use. But many times as you heard from Dr. Mullin and Dr. Woodcock this morning they were developed without the input of patients.

And a perfect example of that is in depression where the endpoint that is accepted in clinical trials is a clinician-reported endpoint. And to folks like myself that are sort of steeped in measurement science we kind of scratch our head at that and wonder, well, why aren't you talking to the patient because they're the ones that experience this every single day.

So, we don't just stop once we get the list of symptoms. We don't just take that list and develop the instrument and say, okay, here you go, pharma, or here you go, FDA. We

actually then have to go test it in more patients.

And we do this very iteratively over a long period of time to make sure that we have a solid signal that we can pick up whether drugs are actually impacting the things that you're feeling.

So, as you can imagine there are challenges and there are also some successes that I'll share with you. One of the challenges has been sort of more on the administrative side. We've run these consortia and they consist of the pharmaceutical companies. In the PRO Consortium that's 25 of the biggest pharmaceutical companies in the world.

We spend a lot of time just working through legal agreements trying to get these projects underway, sometimes almost up to a year, and that's just, quite frankly that is adding too much time to something that is very serious.

We also have encountered in some

instances, not in all instances, but some delays getting response from the FDA on some of the stuff that we're trying to do. And they're certainly aware of that and taking steps to try to get us feedback in a more timely manner.

One of the success stories that I'll just share with you very briefly, and then we'll get back to the important part of this, is we recently had an RA consensus development meeting. There was quite a lot of talk about well, what should we be measuring as a patient-reported outcome in RA. And for years fatigue was off the table. The FDA didn't understand what that meant, no one could define it, but all the patients told us that they experienced it. And so we finally have gotten to the place where we're now going to consider fatigue and go down the path of developing a way to measure fatigue. And a lot of people have already done that. We're looking to tap into those resources. Dr. Woodcock was at this all-day meeting so that shows you sort of the

gravity of the situation that we're facing. We had some of the world's leading experts there talking about RA. We also had patients there talking about their experience.

So, I just want to I guess convey to you that there are those of us that are out there trying to wave the flag for the patient in developing new endpoints. And there's a lot of work to do obviously, but I thank you all for your comments and your time today.

(Applause)

MR. FREY: Okay, we have a few public comments on this particular topic. So we'll go first to these and then we'll get back to the disease-specific comments. So if Julie Flygare can make her way to the mike. Oh, got it. How about Stacy Kane.

MS. KANE: Good morning. I want to thank the FDA for holding this Patient-Focused Drug Development Initiative, the esteemed membership of the panel and the Crohn's and Colitis Foundation of America for allowing me

to be here today.

My name is Stacy Kane and you wouldn't know it to look at me, but I am but one of the hundreds of thousands of people who suffer from ulcerative colitis, or UC, which like Crohn's disease, is an inflammatory bowel disease. I was diagnosed over 5 years ago after the birth of my second child. And while I'm not here to suggest that my disease is more worthy than others, I simply want to thank the FDA for pursuing the path of soliciting patient input.

Ulcerative colitis is an autoimmune disease whereby the body attacks my large intestine. This disease currently has no cure except for removal of the entire large intestine. Its symptoms include uncontrollable frequent bloody diarrhea, abdominal pain and cramping, bowel incontinence, exhaustion and more, and can only be controlled through a trial and error of medications.

As patients the best we can hope for is remission of our symptoms. I am but one of the lucky ones I presume as I've been able to manage my symptoms using the maximum dosage of mesalamine, a plethora of supplements and a stringent diet. Still, the disease is ever present.

The impact and manifestations of this disease is profound. The uncertainty of not knowing if the disease symptoms will recur is in many ways life-altering. And while you might consider me in remission I still suffer from flares or a resurgence of symptoms that can be so debilitating I am unable to even walk my children one block to school.

My most recent flare occurred in April and after yet another 4-month course of steroids, I realized that this disease does progress over time and many patients like me find that they must consider a more complex regimen of medications.

I will go very briefly through this,

but for ulcerative colitis there are five classifications, 5-ASA which is what I take, mesalamine which are not even specifically approved for ulcerative colitis but which our gastroenterologists do prescribe because they do work, steroids like prednisone which have some immediate impact but have significant long-term and short-term side effects, immunomodulators like 6MP which I have tried, antibiotics which I've tried, and biologic therapies of which Humira is the most recent drug that the FDA did in fact approve for use in ulcerative colitis.

Biologics really are the last call for ulcerative colitis patients, and while I have not yet tried them I'm sure they're in my future. And while I've worked hard over the last 5 years to try to obtain remission and I've tried four out of the five classifications of drugs and I don't tolerate much more than what I'm doing right now, I do hold hope that the FDA, in conjunction with patient advocacy groups

and patients and drug manufacturers and all of the stakeholders in this, can in fact provide us some form of relief for all of the conditions for which we suffer.

And I just want to thank you for pursuing this and I look forward to the future and what you will accomplish.

MR. FREY: Thank you. Eric Gascho from the National Health Council.

MR. GASCHO: Hi, I'd like to first start by thanking the FDA for putting this on and just for all the work that you've done to get this new process established is something I think that's really exciting for a lot of folks that are in the room.

I'll make a few very broad comments. A lot of them have already been mentioned today but I would like to underscore them. First is as you start to put together these meetings, as has been mentioned often here, that depending on what disease you're looking at there's a broad range of patients whose views would need to be

incorporated into these. For progressive diseases if someone is towards the beginning of it or if someone has been living with it for 10 years will have a very different view on benefits and risks.

So it's really important to ensure that as you're inviting patients to come in and share their views that you have a whole host of a wide range of folks also. Some will be affected differently depending if it's a man or a woman, different ethnicities will be affected differently. So make sure you understand how these types of things can affect folks living with the diseases as well.

Also, while no one can express the views of living with the condition more than a patient or a caregiver, also remember the role that patient advocacy organizations can have as well. They'll often have a more holistic view of how a wide range of people can be affected by them.

Finally, I had one other thought.

It's been mentioned a few times that these meetings are only one way that patients and patient organizations can interact with FDA. I would encourage you to develop and communicate a more formal process for how patients and patient organizations can interact with the FDA, particularly with the review teams. So, thank you.

(Applause)

MR. FREY: Thank you. Janet Long. Okay, you're ready for that other lineup? All right. Okay, Patricia Gibson.

MS. GIBSON: I'm Patricia Gibson. I represent the amyloidosis support groups. We have 200 members with familial amyloidosis and more than 1,200 with primary amyloidosis.

Twelve years ago last week my husband died of familial amyloidosis and my 7 children and 16 grandchildren are all at risk.

Amyloidosis results when the amyloid protein misfolds and builds up in tissues in one or more organs. It's often

compared to logjams piling up and interfering with and eventually stopping the function of an organ. The heart, the kidneys, the nervous system, the gastrointestinal tract are most often affected but it can appear in almost any organ including the skin or the eyes or the tongue.

Hereditary or familial amyloidosis is found in nearly every ethnic group. More than 100 variants have been discovered. If you are of Portugese or Swedish or Japanese or Irish or French or any Mediterranean area we have a variant for you. About 4 percent of African-Americans carry a genetic variant.

The onset of symptoms also varies beginning in the early twenties and some variance in that until the fifties or sixties in others. In the African-American variant it's very late onset, when people are over 60 years old. Their cause of death is cited as congestive heart failure without amyloidosis having been recognized as the basic cause.

DNA testing pinpoints the diagnosis and the particular variant. Whole families are affected, with each child of an affected parent having a 50/50 chance of having the gene. It's estimated that more than 2,000 Americans have familial amyloidosis although a great many of them are never diagnosed.

Primary amyloidosis shows the same initial symptoms but primary is a plasma cell disorder which occurs randomly in the general population. The estimate is 8 people in 1 million. The deposits in this type are made up of light chain proteins. Again, the diagnosis is difficult and long. Am I already into my 2 minutes? Sorry.

This is a debilitating, wasting, systemic disease. It occurs in all organs. No institute at NIH owns us. We are spread through them all. The patient has carpal tunnel, dizziness, numbness, tingling in the hands and feet, fatigue, indigestion, his heart becomes hard, he can't work and eventually he

can't live.

I'm sorry, I have more and I will just submit my papers to the committee. Thank you.

MR. FREY: Thank you.

(Applause)

MR. FREY: Amy Squires.

MS. SQUIRES: Good morning, my name is Amy Squires and I'm the chairman of the board at the CFIDS Association of America which is working to make CFS, ME/CFS, chronic fatigue syndrome, whatever you want to call it, widely understood, diagnosable, preventable and treatable.

We applaud FDA's public affirmation that CFS is a serious and life-threatening condition as stated at a recent CDER stakeholder call and again at the October meeting of the federal advisory committee. This recognition signals hope to the millions of Americans affected by CFS and it signals opportunity for researchers in industry and academia.

CFS represents a vast unmet need and large potential market. We applaud FDA's inclusion of CFS on the preliminary list of topics for the PDUFA meetings and urge you to include it on the final list.

CFS needs your focus. There has never been a systematic effort to identify effective treatment and there remains no single or polypharmacy regimen that has been shown to treat the symptoms or modify the disease.

In the void, patients and their healthcare providers try to cope. On the online forum Patients Like Me people with a diagnosis of CFS report using more than 800 treatments. That's a lot of trial and error, a lot of risk with possibly no benefit and a lot of expense in our healthcare system.

CFS meets all published criteria for the PDUFA mandated meetings. We believe a meeting could focus on three topics in particular, the types of therapies now being used, the severity of the condition and relative

risks and benefits that should be viewed as tolerable in the regulatory environment, and a greater understanding of the measures of benefit that matter most to patients. Such discussions would have great benefit for drug discovery efforts and the regulatory decisions as ME/CFS research advances.

On a separate but related note I'd like to mention one other thing. We're a founding member of the Chronic Pain Research Alliance and we'd like the FDA to also consider holding a PDUFA meeting dedicated to comorbid disorders. The preliminary list reflects a lot of related conditions and it makes sense to look across those as well as at them individually. Thank you very much.

(Applause)

MR. FREY: Thank you. Steve Gibson.

MR. GIBSON: Thank you. My name is Steve Gibson with the ALS Association. We want to thank you for listening to us today. We've

been speaking to you all for about 2 years now and we look forward to continuing our discussion.

I also want to thank Tom, Mark, Cathy and Scott for taking time out of their day to talk to you about ALS and how horrific it is to educate you.

Today I'm asking for two things. One is to urge you to have a meeting with ALS community for ALS patients, not just the few that are here today, to really come and share their views and their difficulties through life. I'm not sure if you know but there's a higher incidence of veterans who have ALS and we need to really stop and end this problem.

The second thing I urge you to do is when you do publish a list to have an asterisk on that list to say what that really means. On September 24th when you published that list you took a lot of hope out of so many patients' lives, I know with ALS, because they thought that was the only thing you were working on.

And on September 24th you also created disease wars because every disease now feels that if they're not on this list that they aren't doing their job. So whether it's on your website, through the Federal Register, have an asterisk and explain that because you do wonderful explanations for us who come today in the room, but if you are someone who doesn't understand what's going on, you really have no hope. Thank you.

(Applause)

MR. FREY: Thank you, Steve. D. Rose.

MS. KERVITSKY: So, I'm not Dan Rose. Dr. Rose had to leave. I'm Dolly Kervitsky. I'm here from the Pulmonary Fibrosis Foundation.

Pulmonary fibrosis is a broad spectrum of diseases. It is not just one disease. The most common of the pulmonary fibrotic diseases is idiopathic pulmonary fibrosis. It affects between 150 and 200,000

Americans. There are more cases obviously worldwide. About 40,000 people die every year from this disease and 50,000 new people are diagnosed. There are no FDA treatments and nothing has been shown to be effective in improving quality of life.

Quality of life in patients with this disease is severely impacted. They are so incredibly breathless. This breathlessness progresses to the point where activities of daily living, simply breathing, becomes work. So it is a very difficult disease to deal with for patients and families.

There's also a hereditary component of this disease that is not well understood. Dr. Rose who was here from the foundation has -- his family has been severely impacted by this disease as is another one of my colleagues, that this disease affects families, and it affects them continuously.

We really like to hear what everybody is saying about taking a collaborative

approach and using this cluster effect for the FDA to look into these diseases. Many of these diseases, they all affect -- pulmonary fibrosis has an autoimmune component as well. So genetics, autoimmunity, all of these things tie together.

All of us in this room are in this together and we really would like to see more of a collaborative approach in the pharmaceutical industry as well as the advocacy industry and our medical researchers.

I think that's all I have to say. That was quick.

(Applause)

MR. FREY: Thank you. Teresa Barnes.

MS. BARNES: I love that woman. My name is Teresa Barnes. I'm with the Coalition for Pulmonary Fibrosis. I'm also on the board of directors of the American Thoracic Society.

And you may have caught an article in the New York Times a couple of years ago that

was on the human body, and had different organ systems and diseases that affect people. And there was one organ that was missing. A little conspicuous but the lungs were not included. So I guess no one really needs to breathe since the New York Times didn't include it.

At any rate, you know, lung disease is on the rise in this country almost across the board in every lung disease that there is. There's almost no life-saving treatments and very few options for patients. It is absolutely devastating. Imagine not being able to breathe and the rest of your life really doesn't matter if you can't breathe.

And in the last 15 years Dolly was talking about pulmonary fibrosis. That's a disease that's devastated my family. We've lost five people in 15 years. My generation is now at bat. My 2-year-old daughter is high risk for this disease. There's no way to survive it. Usually people die within 2 years. In my family they typically die within a year

and a half. It is absolutely life-altering, life-changing, life-threatening.

In the last 15 years almost a million people have died from this disease. There is no treatment. The FDA actually turned down the only treatment that might have been approved by now. The rest of the world has approved it, the European Union included with Japan, I believe Korea and just recently Canada. So our patients are leaving the country to get care.

At the Coalition for Pulmonary Fibrosis which I helped create with a group of doctors and other experts 12 years ago, we are desperately trying to give patients hope. And I will tell you that the creation of this initiative is key to that. And for all of our patients regardless of what they suffer from, if you take that, you take everything.

So, I would say to you thank you for hearing our patients because I think if we ask the group most people would say that they don't feel that their patients are being heard. So

thank you for listening.

And I would ask you if you would please consider including pulmonary fibrosis. If it's a category of interstitial lung diseases or fibrotic disease that's great, the more the merrier. We all need to win here. We're all on the same team really.

And I would tell you that there's a lot of discussion right now in areas of fibrosis across organs as an example. Many diseases have a scarring process. So if you would consider looking at maybe a wider spectrum as a few people have mentioned so that more diseases can be discovered, maybe treatments that will save lives in a much shorter time span. Thank you very much.

(Applause)

MR. FREY: Thank you. Kate Ryan.

MS. RYAN: Hi, my name is Kate Ryan. I'm with the National Women's Health Network and we're a non-profit membership and advocacy organization that works on a broad range of

women's health issues.

One of our services is a clearinghouse where women actually call us and they tell us about a diagnosis or ask questions and get information sometimes about women-specific diseases but also about women-specific concerns about diseases that affect both men and women. And then we bring those voices to the FDA.

So today I'm going to highlight a few of the diseases on the list that we've worked on and heard about, and an overarching issue that's been indirectly mentioned a couple of times today. Although for example heart disease is the number one cause of death for both women and men, women are still underrepresented in those trials. Women have different symptoms and later onset than men of many cardiovascular diseases, so it's essential that women are included in discussions about patient-reported outcomes for these diseases and that the gender difference in disease

experience will be reflected. And that's true of many of the other non-gender specific diseases that you've heard about today, some of which disproportionately affect women and affect them differently.

Dr. Woodcock this morning mentioned obesity. And I and the Network have been involved in recent efforts to improve patient-reported outcomes and obesity drug development. This very diverse group of stakeholders including patients and consumers and physicians and industry had a whole lot of good ideas that could be useful for patient-reported outcomes.

But one of the main takeaways was that patients were asking for patient-reported outcomes and endpoints in trials that actually measure improvements in their health and quality in life that matter to them. So, we'd really like to see them included in the trials so that there's specific data for drugs to treat this.

And lastly is female sexual

dysfunction which was on the list. The cultural impact and profitability of Viagra means there's a huge interest in developing a drug treatment for women. But companies have been unable to identify a population of women for whom their drugs work better than the placebo, probably because measures of physiologic response don't adequately reflect the outcomes that matter to women. And this is true in other areas when we're talking about feeling and function. Just because there's supposed to be a physiologic response with a drug and they see one, that doesn't mean that people or in this case women will feel better.

So we have serious concerns about the way it's been approached and whether drug development is even the best way to go about addressing women's problems with sexual satisfaction. But if there are going to be safe and effective drugs developed then patient-reported outcomes are essential. There should be an open and multidisciplinary

exploration of women's experience with the problem and their definition of success, and that would benefit everyone.

I'll finish up just by saying we want drug development to meet women's needs and the FDA review process to reflect women's concerns. And I'd say that the Patient-Focused Drug Development Initiative should balance the serious and respectful incorporation of patient input with a rigorous science-based review.

To end with a cliche, women have answers to the age-old question what do women want. Just ask us. So we'd really like to be involved in this. Thank you.

(Applause)

MR. FREY: Thank you. Cynthia Bens.

MS. BENS: Hi, everyone. I'm Cynthia Bens. I'm the vice president of public policy for the Alliance for Aging Research but I'm here representing a coalition of 50 other organizations that we chair called Accelerate

Cures and Treatments for Alzheimer's Disease. We've been very involved in the process for the past 2 years but I'd also like to call attention to some of the work that ACTAD has done over the past 6 years working directly with the review divisions at FDA in taking up some of the issues that are important.

And Dr. Pariser mentioned some of them earlier today, clinical meaningfulness and in particular clinical trials have been challenging for Alzheimer's in phase II. And it has a lot to do with endpoint selection, biomarkers and making sure the science is there to support that.

We feel that the Agency has been very responsive in coming to grips with how they would manage risk and benefit of new treatments for some of the biomarker-selected populations like ApoE4 carriers or people with familial Alzheimer's disease. And we get the impression that there's a very high level for acceptance of risk in those populations, but there's also

a lot of people that are just going to develop Alzheimer's disease because they live a long enough life to develop it. And how the Agency is going to assess risk and benefit in that population is a little unclear.

So there was a bit of disappointment in the Alzheimer's community that Alzheimer's wasn't on the list given that more than 5 million people have Alzheimer's disease and that number's going to grow with the aging of the population.

But we are supportive of the concept that other people have mentioned today of clustering diseases. But I would take that a step further and not only use the broad four criteria that were used to select the individual diseases, but any feedback that we could get from the review divisions on particular aspects of the disease that can help us as patient advocates really get at how we can properly provide you with the information you need, particularly in areas where -- Dr. Woodcock

mentioned this morning some people are afraid to go across the Chesapeake Bay Bridge, or some people bungee jump off of it.

I don't think the older population is any different than that. And so I think that people who are potentially just going to live long enough to develop Alzheimer's disease should have the opportunity to express the types of risks they would be able to accept with new drugs along with the benefits. So, thank you very much.

(Applause)

MR. FREY: Thank you, Cynthia. Brian Rosen.

MR. ROSEN: Good afternoon. I'm Brian Rosen. I'm with the Leukemia and Lymphoma Society. We appreciate the opportunity to participate in this patient stakeholder meeting.

Just a few comments. Dr. Woodcock mentioned this morning the need for a broad set of human experiences. We're well-positioned

at LLS to provide feedback on the needs of patients with blood cancer including the impact of disease on patients, the spectrum of severity of the disease, and the measures of benefit that matter most to patients in the effectiveness of existing treatments.

We agree with FDA's decision to apply the several criteria that you outlined in the Federal Register and many blood cancers qualify for inclusion on the list. I will say that blood cancers do affect functioning and activities of daily living.

There's a very wide variety in severity of disease. Certain of the blood cancers such as myelodysplastic syndrome and multiple myeloma have a particularly severe impact on specific populations like the elderly while some forms of acute leukemia appear most often in children.

You have over a million people in the U.S. that are afflicted with blood cancers. Each year over 140,000 Americans are diagnosed

with blood cancers, representing 10 percent of all cancers.

LLS agrees with many of the other advocates this morning who have suggested that FDA revise the final list by creating 20 broader disease states. So you would have including areas such as cancer or neurodegenerative disease, cardiovascular disease, autoimmune disease. This might help eliminate the impossible task of trying to prioritize 7,000 distinct diseases and would ensure that a broad base of patient stakeholder voices are heard.

Importantly, LLS is embarking upon a strategic initiative to work with blood cancer patients to collect, aggregate and analyze patient-reported outcomes including some of the things that were discussed this morning, clinical manifestations of the disease, impact upon daily life, disease progression, effectiveness and clinical impact of the therapies as well as variances within different subpopulations.

So we welcome the opportunity and we welcome input from the FDA on the design, on the implementation of this type of registry so that it can really provide the maximum benefit to all stakeholders.

Again, we thank you for convening the meeting. We look forward to participating in all steps along the way. Thank you very much.

(Applause)

MR. FREY: Thank you. Percy Leung.

MR. LEUNG: Hi, I am representing cholangiocarcinoma.org. I'm a patient as well. There is about 8,000 new cases per year in the United States, 3,000 in UK and more than 10,000 new cases especially in Asia.

So this disease can be chronic. You are looking at a patient who survived this disease for 4 years but I am one of the very, very few lucky ones. Most of them are diagnosed in advanced stage, stage IV, and the only hope they have is a systemic chemotherapy which is borrowed from pancreatic cancer or colon cancer.

And there's no standard therapies for this kind of cancer.

This cancer can also cause bile duct cancer. It's extrahepatic or intrahepatic. And the symptoms are chronic. Like me, I can move around but am just a little bit tired. I am on systemic chemotherapy. Who knows how long I'll last. But the most important thing is the systemic chemotherapy that is -- there's none for the advanced stage cancer patient.

And I hope that the FDA can at least look into biomarkers. There are currently no accurate biomarkers for diagnosis and prognosis and I think because of the chain, it's genomics and I hope that is the way you can help the patient who is more unfortunate than me. They can last for a week, a month or a few years.

The most important thing is for the caregivers. The caregivers of this disease is pretty frustrated because of the psychological and the physical caring of the patient because of their uncertainty about what will happen and

why. So I just hope that your panel, FDA, will consider cholangiocarcinoma as one of your disease studies. Thank you.

(Applause)

MR. FREY: Thank you. Carlo Rago.

MR. RAGO: I wanted to thank the FDA for their leadership, the patients and the advocates for their participation. I believe this program will have a profound impact not only on the speed of therapeutic development but also the quality.

So my name is Carlo Rago. I'm the scientific advisor for the Duchenne Alliance which is 37 foundations. It's a global network of foundations dedicated to conquering Duchenne. I'm a founder of OpenOnward as well which builds software to expedite scientific process.

So, for each particular drug asset and each particular disease for each particular subcategory and of course increasingly for each particular genetic alteration and for each

particular regulatory decision the purpose of this is -- of this program is to understand -- for all stakeholders to understand what is the permissible risk for a go or no-go decision.

And there's been a lot of talk about aggregation and categorization of diseases into groups. I think that's great. We'll have more representation instead of the list of 20. We were surprised that there were no muscular dystrophies on the list to begin with.

So I think aggregation is great in the sense that you can be more inclusive but I think the primary purpose here is to bring really high resolution to the particular instance when you're sitting across the table from somebody that's trying to have a drug asset move forward.

And so there are two things that I'd recommend. One is to publish exactly the process that you use to review and determine these decisions such that the patients and the advocates can participate more thoroughly and

more effectively. So, if we publish that list I think we can help you help us more.

And the second thing is that, you know, while we may take testimonials whether it's video or text or otherwise that's a good general backdrop but I think perhaps maybe we should have -- maybe the FDA should invite patients to sit at the table for each of these critical decisions at those critical time points.

I think you'll have overwhelming support and participation in that particular event. And maybe that's the best way to overcome the nuances of all of these subcategories.

And I represent Duchenne and of course it's the second largest gene in the genome and that's why there's so many foundations, genetic alterations, immunogenesis, inception. It's 1 out of 3,500. It's a great model for studying other diseases. We're really pushing platforms, novel drug platforms forward. So

everything that we're addressing helps the greater community. And that's about it.

I think the most important thing is to invite the patients to participate in those nuanced decisions. So thanks for your time.

(Applause)

MR. FREY: Thank you. Janet Long.

MS. LONG: Quick correction. I don't represent CCFA but I'm sure they are a fine organization.

I'd like to thank you for the privilege to be here as the representative of the US Hereditary Angioedema Association and as a hereditary angioedema patient. HAE is a rare, debilitating and potentially life-threatening genetic disease that causes attacks of swelling of the hands, feet, face, abdomen and larynx.

Abdominal attacks involve severe pain, nausea, vomiting, dehydration and diarrhea that render a patient unable to function, and the swelling can last for 3 days.

As a mother with severe HAE attacks I was often relegated to watching my children through the bathroom door as they played, unable to move from the cold tile that kept me conscious through the worst hours of an excruciatingly painful abdominal attack.

Of greatest impact for an HAE patient however is a swelling attack of the larynx or airway. Our community of HAE patients and their families live with the daily fear of an airway attack, and the frightening prospect of death by asphyxiation is never far from our minds. Indeed we continue to learn of fatal HAE attacks, one just 4 weeks ago.

HAE symptoms manifest differently in every patient, even within the same family and even during different times of one's life. It equally affects all races, all ages, both men and women, though women tend to suffer more severely.

The rareness of HAE has resulted in delayed and inaccurate diagnosis. We now

recognize that HAE is actually a pediatric disease and more education and awareness is needed to ensure an early diagnosis in affected children.

A study of almost 500 patients concluded that HAE has a significant effect on physical and mental health, negatively impacts education, career and work productivity, and creates a genuine economic burden.

Because HAE is a genetic disease each child of an affected parent has a 50/50 chance of inheriting the condition. Safe and effective HAE therapies only became available in the U.S. in late 2008. And while there are now therapies available none has been approved for use in our most treasured population, children.

There is still a desperate need for research into the cause of and treatment for a subgroup of patients whose swelling is not caused by C1 inhibitor plasma protein deficiency. And even HAE patients who have

access to therapy are not necessarily receiving the most optimal treatment regimen today.

Great strides have been made in bringing forth new therapies for rare diseases like HAE but we are aware that the story does not end there. This meeting and those in the future offer a unique opportunity for HAE patients to contribute to the pool of knowledge that you seek and we urge you to keep hereditary angioedema on your list of disease area nominations. Thank you.

(Applause)

MR. FREY: Thank you. Allison and Jack Willis. They might not be here anymore. Oh, okay.

MR. WILLIS: Thank you for allowing public comment. Hi, my name is Jack Willis. I am here with my twin brother Nolan. We have Duchenne muscular dystrophy. We are 11 years old. Our current life expectancy is 20 years old. You do the math.

We represent a population of boys

who are dying waiting for a treatment. My brother and I are in a clinical trial. At the beginning of the trial in August 2011 we could walk. Now, neither of us can.

Our disease causes us to all deteriorate at different speeds. The older we get the more people have to do for us. I will lose the ability to feed myself among other daily activities.

Please consider pediatric neuromuscular diseases on your list and help us live longer. Thank you.

(Applause)

MR. FREY: Thank you. It looks like we have about four other folks who aren't on the slide. We'll go first with Peter Reinecke from the Chronic Pain Research Alliance. He left? Okay. How about Joseph Vassalotti from the National Kidney Foundation?

DR. VASSALOTTI: Thank you very much. I want to thank the FDA for this really innovative, fabulous meeting today. And

hearing some of the poignant stories of the patients, as a physician I feel humbled to speak before you.

I want to thank you for this time to represent the National Kidney Foundation. It's an organization of 25,000 patients and families with kidney disease. It's also a mix of a professional organization and a patient advocacy organization. It includes thousands of healthcare workers who care for the 26 million Americans with chronic kidney disease.

I'm going to keep my comments brief and I'm going to restrict them to the two subject areas that are potentially topics for future meetings. That is glomerulonephritis and transplantation.

So first on glomerulonephritis, what is it? It's inflammation of the small functional units of the kidneys. We have about 1 million in each kidney if we're healthy.

And why is this important? Why is a patient-centered approach or patient-focused

approach to drug development important? Patients experience edema, swelling, which may involve the abdomen, which may also involve many other symptoms like fatigue, increased risk of cardiovascular disease and blood clots, and of course progression of kidney disease to chronic kidney failure which requires dialysis and kidney transplantation.

Currently there are very few FDA-approved therapies for glomerular disease, glomerulonephritis and we think there are tremendous opportunities for increased efficacy to prevent some of those symptoms and complications that I mentioned. And also increase patient safety, decrease side effects because most of the drugs that physicians use today suppress the immune system in a general way.

If the kidneys do fail that brings me to transplantation, the second topic. So of course all solid organ transplantation requires immunosuppression to prevent rejection

of the solid organ, and kidneys are just one of many of the organs that are currently transplanted in medicine today.

Unfortunately why this is important for patients is that the current medications in use have a lot of side effects, chiefly infections, malignancies, chronic diseases like diabetes can develop as a result of the immunosuppressive medication, high blood pressure, high cholesterol and there are many others. So we think that patient-focused drug development is exciting in this area because particularly it can help to limit the side effects that patients experience.

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

(Applause)

MR. FREY: Thank you very much. I have a name here, David Gold, but there is an email in parentheses behind the name. I just want to make sure you did want an opportunity to speak.

MR. GOLD: I planned on just sending in an email because I wanted to make sure everybody had time to speak that wanted to. But if there is time I have a few comments.

MR. FREY: Go right ahead.

MR. GOLD: As somebody who has been a patient before and of course many family members have been patients I can tell you I just, I applaud the efforts of all the patient advocacy groups. But as a scientist and a statistician currently working in industry I want to make sure it's clear that there's no conflict of interest in what I'm about to tell you.

There are many challenges moving forward in collaborating together, and I think the more that we're talking and sharing with each other about how we can move forward good objectives and avoid delays and risk to a process that I think that you're interested in seeing be successful. I think that's really great. So the more that you share with us as to how you'd like to see us involved and how you'd like

to see us help.

Patient-reported outcomes, there are statistical challenges in using them for a variety of reasons. How you collect the data, how you present the data, those are challenges even for scientists. I can only imagine what families who have sick children and are burdened might be going through in collecting that kind of data and reporting it. So standards in place that are achievable for patient advocacy groups supporting rare diseases largely run in an unfunded way by families. Those sort of interactions, that kind of information-sharing would be very useful.

MR. FREY: Thank you.

(Applause)

MR. FREY: Last we have Amy Melnick from the Arthritis Foundation.

MS. MELNICK: Wow, a lot of pressure being last. I'm between you and lunch so I'll try to be quick.

Good afternoon. My name is Amy

Melnick and I'm the vice president of advocacy for the Arthritis Foundation. The Arthritis Foundation is the largest national non-profit patient organization that supports patients with arthritis through research, public health and advocacy.

We welcome the opportunity to provide comments to the FDA on this critical issue. How to involve patients more in the drug development process and how to include patient input into benefit-risk decision-making. We thank the FDA and Dr. Lundy in particular for the work in rheumatoid arthritis and the work group within the PRO Consortium.

However, the foundation would like to express our concern with the process that the FDA used in selecting the 40 diseases for prioritization in developing this request for comments. Little or no information was provided to the public regarding how these specific diseases made it onto the list or not. We respectfully request that serious

reconsideration be given to this set of initial diseases and we're proposing that osteoarthritis be added to the list.

Why osteoarthritis? Because it clearly fits the FDA-proposed inclusion criteria. Osteoarthritis is a serious, painful, chronic disease affecting 27 million Americans. According to the CDC, it's the most common cause of disability in the U.S. Symptomatic, very painful and mostly affects the hands, knees and hips.

As the most common cause of disability, OA clearly affects functioning and activities of daily living. It results from a thinning of cartilage caused by injury, inflammation, age and genetic factors. The breakdown of cartilage causes the bones to painfully rub together all the time.

Symptoms of OA include joint pain, aching, stiffness and swelling resulting in decreased function and mobility. Symptoms of osteoarthritis typically first begin after age

40 and affect a large working age population and also the elderly. Clearly impacts a broad range in terms of size of the affected population.

We believe it is unacceptable that osteoarthritis places such a significant limit on daily activity and quality of life. About 25 percent of people with knee osteoarthritis have difficulty doing major daily activities such as walking, working, climbing stairs, kneeling, and bending due to the pain of OA and the loss of function. OA results in approximately 632,000 joint replacements each year.

Finally, of most concern to the foundation in terms of today's meeting is that there is no disease-modifying therapy that slows or stops the progression of osteoarthritis. Available therapies include pain medication which only mask the painful symptoms of OA but do nothing to improve function.

Patients with severe OA live in

constant pain and are likely disabled. Their tolerance for risk is much higher than those with mild OA.

In closing, the Arthritis Foundation respectfully requests that osteoarthritis be added to the FDA's first set of disease areas of focus. We look forward to working with the FDA as you continue to implement these patient-centric provisions of PDUFA V. Thank you.

(Applause)

MR. FREY: Thank you. We have Miriam O'Day from the Alpha-1 Foundation.

MS. O'DAY: Thank you. So I'm going to represent two organizations here very briefly. First of all, the COPD Foundation. COPD, being the third leading cause of death, is not represented on the list. But we would like to note that progress has been made through the Biomarkers Consortium that the COPD Foundation has been able to form and work very collaboratively with the FDA on.

We would urge you to have us join some of the other lung diseases that have been noted and take a look at COPD if you take a look at body systems.

Secondly, on behalf of Alpha-1 and the Alpha-1 Foundation, Alpha-1 antitrypsin deficiency is a liver disease. It's a conformational protein folding disorder. What happens is in the pediatric population they're born with severe cirrhosis of the liver. There's no treatment aside from transplantation.

In the adult population it manifests as a lung disease and the treatment is to have weekly plasma infusions. And we're hoping for next generation drugs and advances.

We commend you for putting Alpha-1 on the list. We've worked collaboratively with the FDA for many years. We've shared with some in this room and would be happy to share with others our model, our liaison relationship, the critical issue workshop series that we've been

through and some of the investment that we've made in translational research and been able to advance the area of translational disease treatments in Alpha-1.

I would say that it's unfortunate. We agree with most of what's been said here today but it's unfortunate that we're in the middle of disease wars here because in fact this is pilot, this is talking about models and this is the opportunity for us to come forward, share what's been successful and figure out how to be more successful into the future.

So I would like to go on the record and disagree that Alpha-1 should be a subcategory of COPD because our untreated population is really the pediatric liver disease population. Thank you very much.

(Applause)

MR. FREY: Thank you. We have a comment here? Would you mind just introducing yourself and your affiliation?

MS. SCHWEITZER: My name is Mary

Schweitzer. I was a professor of history with a Ph.D. from Johns Hopkins and a rising career when I was felled with what is laughingly called chronic fatigue syndrome in 1994.

I did not suffer from fatigue. I had a blackout in my office. When I came to I couldn't understand a word of what was in the papers in my lab. I couldn't move at first. Let me describe some of the symptoms that I then lived with increasingly because I had a progressive form of the disease.

Actually what I have is myalgic encephalomyelitis. I fit the definitions going back to the nineteen fifties. Unfortunately that has been subsumed under this umbrella thing chronic fatigue syndrome which you get laughed at when you say that's what you have. And forgive me for being tense, but I'm used to being laughed at by people in the government.

Okay, my symptoms. Ataxia, expressive dysphasia, dyslexia, memory loss, blackouts, absence seizures, disorientation,

massive confusion. When I was still able to walk I poured an entire pot of coffee into a silverware drawer absolutely convinced it was a cup. I didn't know how to put a seatbelt together. My daughter had to put me in the car and put the seatbelt on me because I didn't know how to do it.

I had pain behind my eyes and in the back of my neck and a stiff neck 24/7 every minute of the day and headaches the size of migraines. I know this because I used to have migraines but they were on both sides of my head, not just one side of my head. And I had extreme muscle pain.

I am lucky though because since I was a scholar I talked my way into studies. We found that I had HHV-6 variant A which was first discovered among AIDS patients cytomegalovirus, Epstein-Barr, HHV-7. These are all four in a row of -- gamma herpes viruses plus another one. HHV-6 and CMV are in my spinal fluid which kind of makes sense because I have

a lot of symptoms of encephalitis but I'm not allowed to say that because I have chronic fatigue syndrome and that's not encephalitis. And that's why I'm tense. I'm sorry, that's why I'm sort of defensive.

Okay, I'm very lucky because in 1999 I was able to start treatment with an experimental phase III immune modulator. My family pays $22,000 a year for this privilege and I have to take a train up from Delaware to New York twice a week to get it by IVs.

I have lost this drug twice and twice I have been like the Robert de Niro character in Awakenings who knew he was going to fall back into being a blob lying in intense pain in the dark listening to a movie because I couldn't stand the pain and I couldn't understand most of what was said to me. At my worst we have to have seat risers and a shower chair and rails in the bathroom and I have to be helped to do everything because I cannot do anything for myself, not even brush my own teeth.

If I lose this drug that's where I will be again before a year is out. Before a year is out I will back to that condition which is living hell. I say that because I imagine there are people in this room who have unusual diseases and have been living off of phase III or other drugs and lose them mainly because it's a small company that doesn't know how to keep the drug.

And there's reasons for drugs not to be passed, but one of the reasons should not be because it's a small company that doesn't know what the hell they're doing. If the drug is not highly toxic and it's helping me I should be the person who chooses that I get to keep the drug. And that's what I want to say. I want to say it for many people.

And the last thing I want to say is people get this as teenagers. I know people who have had it, they got it as teenagers, they've been living with it and they're in their forties.

I was lucky. I met the love of my life and married him and he's taken care of me through all of this. He has cancer now, bladder cancer, and that's why I was late getting here so now I have to take care of the caregiver and I'm not totally well. But he's taken care of me all this time. I'm lucky.

I have two children, I have two grandchildren. I only had 10 years of a career but it was a great career and I loved it. If you get sick when you're a teenager and you stay sick till you're in your forties you don't have any of that. You don't go to college, you don't meet the love of your life, you don't get married, you don't have a career, you don't have kids, you have nothing. And that's what this disease really is.

And I wanted to make sure you people understood that and understood that whatever's helping us, whether it's rituximab or Gc-MAF or there's other things that are helping different people that don't help me, that help

other people. There's antivirals that help other people that don't help me. We need to be able to use what helps us and don't stand in our way so much please, I beg you.

And please don't take my drug away from me again because I don't know what I'll do if I have to go back down the rabbit hole and be Robert de Niro in Awakenings. Thank you very much.

(Applause)

MR. FREY: Thank you. At this time are there any other comments? Okay. I think from my perspective I want to say thank you. Thank you for coming out here and sharing your perspectives. We've collected a lot of information today and as I mentioned when we started off we have over 400 comments in the public docket. And based on what some of you were saying today we expect more to come in. So November 1st is that deadline.

It's going to take us awhile to get through all this information and come up with

that set of disease areas that we'll be meeting about for the first 3 years of PDUFA V. When we do do that that'll be published on our website but it's going to take us a few months to get through all this information. So, I don't know if my FDA colleagues have anything they'd like to say.

DR. MULLIN: I'll add that it's literally going to be a few short months. We're approaching the end of the calendar year so we can't promise the end of the calendar year. I'm not sure we can get through it all given November and December, you know, being what they are. But we do have a commitment to getting these meetings underway so we have to get this figured out and get that next step moving. So you know that that's going to be a short time but we want to give this due diligence and be careful.

You've heard everything we've heard today and I think you probably appreciate the challenge of coming up with the best approach

that does the most to help the most patients. So we're working on it. Thanks. Thank you very much for coming today.

MR. FREY: Thank you very much.

(Applause)

(Whereupon, the foregoing matter went off the record at 12:40 p.m.)