NWX-HHS FDA CDER (US)

Moderator: Randi Clark
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Coordinator: Welcome and thank you all for standing by. At this time I would like to remind parties that your lines are in a listen-only mode until the question-and-answer session at which time you may press star 1 to ask a question.

Today's call is being recorded. If you have any objections you may disconnect at this time. I will now turn the meeting over to Sandy Kweder. Thank you, you may begin.

Dr. Sandra Kweder: Well good morning everyone. My name is Dr. Sandra Kweder and I'm filling in at the moment for our Center Director Dr. Janet Woodcock who, unfortunately, had a last minute scheduling conflict. She is going to join us as soon as she can, but I'm going to go ahead and begin our conference call.

Before I do, I thought it would be helpful to you to hear the voices of some of the people who are here in the room with me and who I may call on to help answer questions if that comes about.

So I've introduced myself and I'm going to start by going over to my right.

Dr. Theresa Michele: Good morning, my name is Dr. Theresa Michele. I am a Clinical Team Leader in the Division of Pulmonary, Allergy and Rheumatology Products, which is the division that would review products for chronic fatigue syndrome. In addition, I'm the FDA representative Ex-Officio to the Chronic Fatigue Syndrome Advisory Committee at HHS.

Dr. Keith Hull: My name is Dr. Keith Hull. I'm also in the Division of Pulmonology, Allergy and Rheumatology Products. I work with Dr. Michele and am an alternate on the Chronic Fatigue Syndrome board.

Dr. Theresa Michele: And you're in rheumatology?

Dr. Keith Hull: Rheumatology, yes.

Randi Clark: Hi, I'm Randi Clark. I'm a Public Health Analyst in the Office of Executive Programs and that's in the Center for Drug Evaluation and Research.

Alina Gonzalez: Hi, good morning. My name is Alina Gonzalez and I am a Project Manager in the Office of Executive Programs and in CDER.

Mary Gross: I'm Mary Gross, I'm a Policy Analyst. Also do project management work and will be helping to manage this project. I'm in the Office of Executive Programs.

Dr. Sandra Kweder: And I want to say - I want to thank those three women. They put this conference call together, which is a lot of work. Most appreciated all of you.

Andrea Tan: Hi everyone, good morning. My name is Andrea Tan and I'm from CDER's Office of Planning and Analysis.

Ramesh Menon: Hi, I'm Ramesh Menon and I'm from FDA's Office of Legislation.

Janet Norden: Hi, I'm Janet Norden. I'm the Associate Director for Regulatory Affairs in the Office of Medical Policy in the Center for Drugs.

Dr. Lydia Gilbert-McClain: Hi everyone, good morning. My name is Lydia Gilbert-McClain and I'm the Deputy Division Director for the Division of Pulmonary, Allergy and Rheumatology Products. (Unintelligible), this is a division that we'll be reviewing products for chronic fatigue syndrome. Thank you.

Dr. Sandra Kweder: Okay and that's it for the moment. Let me tell you a little bit about myself as they know who they're going to be listening to for the next few minutes. I am a physician. I'm an internist. My position is I'm a Deputy Director of what's called the Office of New Drugs.

And the Office of New Drugs at FDA has 18 clinical - clinically related - review divisions within it. The division of the Pulmonary, Allergy and Rheumatology and Immunology Products is one of those 18 divisions. I began my FDA career, oh I hate to say it, but about 20 years ago in the Division of Anti-Viral Drugs.

At the time, there were no treatments at all. Well, there was one for HIV. And we didn't call it HIV then, it was just AIDS. And I joined that division and have had many years of experience working with patient groups who are bearing the burden of no therapy to treat their disease.

So I'm really pleased to be here today speaking with you about chronic fatigue syndrome and myalgic encephalomyelitis.

So I'll probably speak for about ten minutes just to frame a few matters so that you can understand a little bit about what we do here at FDA. And then can coach questions accordingly. So I'll speak and then for the rest of the time we'll just take your questions. And we have an operator who can help us do that.

I want to emphasize how happy we are in this room to be here today to begin to explore how best to facilitate development of safe and effective treatment for symptoms suffered by patients with chronic fatigue syndrome and myalgic encephalomyelitis.

We really do - all of us here have had experience taking care of patients with these conditions or know people who have them. We understand your plight and understand your frustration at a lack of approved drugs that can be safely marketed to treat illnesses and conditions like yours especially when there are no alternative options.

What we do - I'm going to take a minute to discuss the role of CDER, the Center for Drug and Evaluation Research, as it pertains to reviewing and approving drugs. CDER, the Center for Drugs, reviews clinical research to ensure that only safe and effective drugs are actually marketed to the American people. Our evaluations ensure that drugs that are ultimately approved meet pretty stringent standards for safety, effectiveness and quality.

And what I mean by quality is, is within the tablet what it says on the label. And it’s just the same every time you put that tablet in your mouth. It's important to keep in mind that, contrary to what many people think, FDA and CDER do not conduct the clinical studies that support marketing.

Other groups do that. Many, if not most drugs that ultimately reach the market, are studied with funding from drug manufacturers. And it's they who give money to academic physicians, academic medical centers or clinicians in the community to conduct the studies that are needed to demonstrate that a drug works and to help understand its risks.

Once those studies are done they're submitted to us and we review the data about the drug in question and look to see if it demonstrates the appropriate risk to benefit ratio. It if does, we approve that drug for marketing. If it does not, we inform the manufacturer about what we think is needed.

We also monitor approved drugs that are on the market for any unexpected drug risks. If a drug is found to demonstrate what we consider to be an unacceptable risk even once it's on the market, we inform the public. We work with the manufacturer to change the label and sometimes we'll even remove a drug from the market, although that's very rare.

So that's kind of the very high level. With regard to chronic fatigue syndrome we are also, as you've heard, an active participant in the Chronic Fatigue Syndrome Advisory Committee or CFSAC to address issues raised by that committee that fall into our purview. We can't address everything that comes up for a discussion in our committee, but there are things that we can contribute where we can contribute to the discussion and advise the committee.

So how does our role impact on activities related to the conditions we're discussing today? I want to be clear once again that we don’t test the drugs ourselves. But our role is to evaluate clinical data received from companies and others like the NIH, for example, in a timely fashion.

For certain diseases, and I give the example of HIV and AIDS, FDA has in the past, taken steps towards making experimental drugs intended to treat life threatening diseases more widely available for severely ill patients as well as towards spreading the review and approval of the applications for these products.

We do this routinely. We do it for many serious and life threatening conditions, not just ME, but very rare diseases, cancers, pediatric cancers. Many, many conditions.

FDA's committed to making promising drugs available to individuals with serious diseases as quickly as possible for the rapid development and review of these types of therapy. For example, you may have heard the term, “the accelerated approval process.” This is in FDA's regulations…this process is set up to increase the availability of experimental drugs and biological products based on findings that are somewhat preliminary, but thought to predict clinical benefit. So, we are talking about clinical endpoints and clinical trials that are thought to ultimately predict more substantial clinical benefit.

To qualify for the accelerated approval program, drugs need to treat serious or life-threatening diseases and provide meaningful and measurable therapeutic benefit to patients over existing treatment. This process has helped us address unmet medical needs and speed the review and approval of applications.

Once a product is approved under accelerated approval, the company is required to conduct future studies to really confirm the effectiveness of the treatment, or the regulations do allow us to remove the drug from the market. And fortunately we haven't had to do that very much at all.

So that's one example of the kinds of things that we can do here once treatments are identified and underway in clinical studies. We have regulatory frameworks that we can apply to help make those products more widely available even when they're experimental, but also in getting to the market quicker.

Now I want to mention that we have heard from some patients who object to us using the term ME/CFS or CFS/ME in the screening of these. I want to make it clear for our purposes relating to drug development, drugs are developed based on quantitative measures that improve symptoms.

We believe that the term CFS/ME is a frame of reference that is intended to be inclusive, but doesn't make any judgment on the cause of different symptom complexes and whether or not the symptoms are best lumped into one or split into different diseases. Again, I want to emphasize that we understand and appreciate your concerns about lack of available treatments for your disease and I personally share those concerns.

Now I know you've asked for a stakeholder meeting with FDA to discuss how we can improve this situation and really what is needed as part of the drug development process to bring safe and effective treatments for CFS/ME to the market. In order to achieve this goal, we are planning to hold a scientific workshop that explores how to identify valid, reliable, quantitative outcome measures to determine if disease symptoms do improve with specific interventions.

The activities we have planned include with starting with conference call just to sort of open the discussion, but on October 3 and 4th there is a CFSAC meeting scheduled where FDA will be on the program to describe the drug review process in more detail so that all the other participants in that process really understand what FDA's role is. Dr. Michele and I will be presenting and available to answer questions of the committee and the community of that meeting.

In mid-November, we are putting together an Excellency in Advocacy webinar that will - that anyone is free to sign up for that is intended to advise

on diverse - advise patient advocates or advocacy groups on how to come together and develop common themes to ultimately further your mutual goals and be beneficial to everyone.

We've done this before, we've held these kinds of sessions, you know, in person, at conferences. We're going to do this one as a webinar, though, because it's relatively short notice and we thought that would allow as many people as possible to participate.

And, finally, in the spring of 2013, CDER will hold a scientific workshop may be a day and a half or two days that will be open to the public. Again, to explore a multitude of scientific issues about identifying valid, reliable and measurable outcomes to determine if disease symptoms improve with intervention. As part of this discussion, we want to hear from academic experts, from clinical practitioners who are taking care of patients with these conditions and patients themselves.

We will set up the workshop to really facilitate that kind of input. We're excited about this dialogue and we hope that you are too and that you see this as a positive step.

I'd like to open the call now to questions from patients and advocates only. And I believe our kind operator will assist us.

Coordinator: Thank you. At this time if you'd like to ask a question please press star 1 on your touch-tone phone. Please record your name when prompted and I will announce you when we're ready for your questions.

If your question has been answered, you may withdraw your request by pressing star 2. Once again, press star 1 and record your name if you have a question. One moment please for our first question.

Our first question is from Robert Miller. Your line is open.

Robert Miller: Yes, good morning everyone. Good morning Dr. Kweder. First, I am Robert Miller and I'm a ME/CFS patient and patient advocate. I find it a good omen today that Dr. Jerome Horowitz, who is the creator of AZT, is being remembered for his work after his recent passing.

I'd like to state that our group made the initial contact with Dr. Woodcock and the FDA to hold a joint ME/CFS stakeholder meeting. I state this as our group has really expanded to working with many other patient groups, patients and advocates. We would like to thank Dr. Woodcock and her team at the FDA for expediting these early steps from our first contact to setting up this new website to doing the webinar and to doing today's call to advance us to the actual joint ME/CFS stakeholder meeting.

There's some key issues I'd like to address, some of them touched on. So I'll make this more of a statement and then if there's time potentially my issues can be addressed. First I'd like to be clear that ME/CFS is a serious complex disease that lacks treatments and suffers from the unwillingness of insurance companies to pay for off label use for drugs that are used to treat or help treat this illness.

They also deny paying for drugs that are in clinical trials. And to list a few drugs there's Valcyte, Valtrex, Vistide. There's IVIG. Recently is Rituxim has started to be used. The only drug in an FDA approved clinical trial for chronic fatigue syndrome is a drug called Ampligen which I've personally been

enrolled in, in two separate clinical trials since 1998 and it's the only reason I can function here today, but at a great cost to my family because I have to pay for the drug.

Ampligen has been given to humans for over 20 years. If there was a safety issue, the trials would've stopped by now. I've been fused with over 50 patients over the years and none have lost an arm or a leg. All the drugs that I've mentioned here have shown benefit to different patients and improved quality of life. And that's a measurement used by the FDA.

We also need to look at the risk-benefit which was mentioned earlier, but it needs to be looked at with the addition of the eyes of the patient's perspective. Unless you've been sitting in our chairs, lying in our beds, or chained to our homes, you really have no idea how to truly measure our quality of life. It really is why we're here today.

We want to help educate you and the latest division that we now sit under, it's why we have - it's why we must have expert ME/CFS clinicians involved and fully engaged in the stakeholder process along with a broad range of clinicians and researchers from immunology to neurology to GI specialists.

In closing, our group feels that it is in everyone's best interest to use a mediation firm like Keystone or Resolve as they are very well-versed in assisting all stakeholder participants with major health issues. And it was mentioned earlier such as HIV and AIDS.

And, once again, I would like to thank Dr. Woodcock and the FDA for expediting the process and getting us to the point to where we are today and having the items set up for us to move forward in the future. Thank you.

Dr. Sandra Kweder: Okay well thank you Mr. Miller. I want to pick up on your comments about measuring what the patients feel and experience.

And we agree that that is one of the biggest tasks for us and is working with people like the patients and clinicians who take care of them with experts in this whole measurement science to figure out what are the questions, what are the things that we need to measure and ask patients about in order to really get to the heart of this condition and understand what the benefits are of a particular treatment if there are any.

It is one of the biggest challenges in this area of investigation is what those measurements are. The good news is that we have a whole group here in CDER whose job is to work with our clinicians in our divisions and academics in our community and company to work through how to put together those kinds of measures so that we are really getting right to core of the disease and measuring what's important to patients.

It's really different than if the doctor thinks the patient does better. You want to know does the patient think the patient's better and be able to measure that well and reliably so that if the drug works we can figure out very quickly.

So thank you for your comments. Very much appreciated.

Robert Miller: Thank you.

Coordinator: Thank you. The next is from Terry Gilmete. Your line is open.

Terry Gilmete: Hi, my name is Terry Gilmete and good morning to you all. And thank you so much for this opportunity to call in. I'm a patient that has had chronic fatigue ME for 27 years and, until recently, I have not been treated.

The insurance - what would I call it? The HMO that I was in, you know, really didn't have anything to help me out and so very, very luckily I feel like I've, you know, come upon the lottery to be working with Dr. (Pierce) up at Incline Village and I'm in the clinical trials for Ampligen and I'm finding that it's kicking in and I'm getting some more energy and I just feel so grateful to have this opportunity.

But I know that there are so many others that don't have this opportunity and it is a great cost to my family as well. I have to travel 250 miles round trip twice a week and rely on family members and friends to be able to get me up there. And I too have to pay out of pocket for this even though I'm not with that HMO anymore and, luckily, my husband is able to hold his job and I'm able to get a little bit of the doctor's cost through his insurance.

But it is a financial burden, not just to myself, but to my whole family and it's of great concern that, you know, so many others don't have access to it. And you had mentioned that, you know, the life threatening diseases get the medications pushed through and, you know, they're finding more and more that there are life threatening aspects to this disease such as heart failure and cancer rates that are higher because our immune systems are compromised.

And so the more and more we seem to be learning about this disease, the more it's coming out that it's much more in a life-threatening category. Not only life diminishing because you're so relegated to bed and to being house bound and to not able to do a lot for yourself. That it has in fact - you know, things have come out to show that it is much more - it can be much more of a life threatening situation than otherwise perhaps thought.

So again I just wanted to put out some thoughts and some comments and wanted to ask, you know, how was it that those with HIV, you know, using Ampligen, how was that put through in order for them to be able to use that medication and have good success with it over the years? How was that process put through at a much quicker pace than those of us with CFS/ME? And I thank you again so much for your time this morning.

Dr. Sandra Kweder: Thank you very much Mrs. Gilmete. Can I just ask a point of clarification? Did you mean how the HIV patients got Ampligen? I don't recall - did you mean AZT?

Terry Gilmete: My understanding is that Ampligen is used for HIV patients as well.

Dr. Sandra Kweder: I think there was one study, a very, very small study some time ago and I don't think it was found out to be very helpful. It was a clinical trial.

Terry Gilmete: Okay.

Dr. Sandra Kweder: But I think - but your point's a good one. And I'll sort of respond to a couple things that you mentioned. We consider your condition to be in the category of serious or life threatening diseases.

Okay, so all of the measures to move things through rapidly, all of the tools that we have here at FDA to try and expedite reviews or expedite development and work with companies to try and encourage them along that would apply to, you know, immediately life threatening cancer, as far as we're concerned they apply to this condition.

This is a serious condition and I just want to make that clear. We consider it in the same category because there are no approved treatments for this condition

and we understand how seriously and severely peoples' lives are impacted by this disease - by this condition.

But since you did ask about HIV, I'll pick up on a couple of things. One of the first things that happened - what really revolutionized the study of HIV, just as an example, was finding something to measure in the clinical trials. In that case they had the, you know, fortune or misfortune to be able to identify some marker in the blood that was predictive of the clinical course of the disease. In the beginning it was a type of white blood cell, CDR lymphocytes.

That was in the beginning. Later, when the virus itself was discovered, we were able to measure the amount of virus in the blood and show a lot of the antiviral treatments decreased the amount of virus in the blood. So the way the clinical studies for HIV are still done today is they are initially approved under accelerated approval by showing over six months that the amount of virus in the blood declines.

They're put on the market, but those studies continue on further to show over time that that viral depression or lowering persists out to several years and that the patients don't develop other illnesses. But that's how it was done.

And again, you know, regardless of what the measure was by advocates and scientists coming together and really probing what's understood about the disease, measures that could be put in - reliable measures put into clinical trials to identify and not just revolutionize the field of being able to find drugs for approval because we have something that everyone agreed with a good measure for the disease. So thank you for bringing up those points.

Terry Gilmete: Thank you very much for your time this morning.

Coordinator: Thank you. The next is from Patricia Carter. Your line is open.

Patricia Carter: Yes, my name is Patricia Carter and I have suffered from ME for 27 years also. I appreciate the opportunity to hear this information today. My question is- are there any other drugs, aside from Ampligen, anywhere on the horizon that the FDA knows about? Are any of the other drugs being considered for treatment of ME/CFS?

Dr. Sandra Kweder: I'm going to turn that question over to Doctors Michele and Hull, who are really the experts here.

Dr. Theresa Michele: So in the Division of Pulmonary, Allergy and Rheumatology Products, which is where all of these applications are housed, we currently have eight open IND's or Investigational New Drug applications to study products for chronic fatigue syndrome.

And, while I'm not permitted to give details about any of those applications, that's the research that's out there currently at FDA.

Dr. Sandra Kweder: Terri, can you say something about, you know, what kinds of products these tend to be?

Dr. Theresa Michele: Many of them tend to be nutritional supplements. Most of the studies are very small, early phase studies. So it's really emphasizing the fact that the research, particularly for drug development in this, this is the very early stages and anything that we can do, as Dr. Kweder mentioned, to jumpstart that process by giving companies good endpoints to measure will really accelerate the process.

Dr. Sandra Kweder: Thanks. You know, and I'm going to follow up on that point. One of the challenges, to try and get the companies interested in investing in products to treat a condition.

One of the things that we've learned from experience is you've got to be able to define the condition well and they need to - they want to know where are the rules about studying it. What am I going to have to show in order to get a drug approved? Because I don't want to invest in a drug that I'm ultimately not going to get approved for marketing. That's not good business for me.

And even if I care about these patients, I have to know what I need to measure. And so that is why we keep coming back to this point of putting together - coming to agreement of what are the things that need to be measured most. So, for example, the word “fatigue.” I would venture that the kind of fatigue that many of you on this call feel is a little bit different than the kind of fatigue somebody who has just been in an auto accident feels or the kind of fatigue that someone who's stayed up all night feels.

There are differences and they're subtle. And making sure we can measure them well is really important. So one of our goals for that meeting in spring is to get companies, and I know some of them are on the phone. We're counting on you to help with this is to really try and bring the science together so we can stimulate that kind of interest and get some of these products - actually some of these products that many of you are taking - tested.

And if they work, let's get them on the market. Let's get them approved so that your insurance companies will pay for it and so that you really understand what benefit you can expect.

Patricia Carter: Thank you.

Coordinator: The next is from Deborah Waroff. Your line is open.

Deborah Waroff: Hi. First of all, I want to thank the FDA and I want to say that one of my childhood heroines was Frances Kelsey and (unintelligible). I have a couple of suggestions to make from personal experience and research.

Number one, I have just completed a trial of GcMAF which is - that's G as in George, C - Charlie, M - Mary, A as in Alice, F - Francis. And that is a substance found in mammals that is related to the D vitamin receptors in some way. I don't really know the full thing, but it has been shown there's research in PubMed on this by Yamamoto, who showed that it can inhibit tumors and have sort of properties.

In my case, what it did and this brings it around to measurements is over the course of the year my end case count which is a very commonly known measure amongst clinicians in this disease, my end case count which had been below normal for ten years receded to two after the gentle administration of the hospitals or special surgery who failed to provide me with any after care.

And I was in terrible, terrible shape. And it receded to two. And after a year on GcMAF which is a weekly injection I am now at 21, the measure being NK cell cytotoxicity. And some of you will recognize that that means I'm in the lower reaches of normalcy. In other terms of measurement, my measure for functionality and whether a treatment's been effective is the salad - whether I am making salad or not is always a good measure because, when I became very, very ill, I became too weak to do this.

And I want to share that, in the last month, I've not only made salads, but I have made guacamole. Now I realize that's not considered a scientific

measure, but you can construct equivalent measures of the activity. Further on the measurement side, I want to say that the other areas, immune counts are probably number one. The NK cytotoxicity's easy to measure.

Number two, we have to work from Myhill and company in England on mitochondrial abnormalities. And these can be measured. Number three, obviously anti-viral, what the virus counts are with anti-viral drugs.

I don't want to go on too much, but I do want to mention a drug I'm most interested in for this disease, which hasn't been mentioned at all, which is Lenalidomide which ironically with my mention of Frances Kelsey who saved this country's children from Thalidomide. Lenalidomide is a derivative of Thalidomide. It is used in cancer treatments. It is restricted to the use of cancer treatments because it has teratogenic effects.

And rather than make sure that people observe appropriate birth control protocols, at this moment it has been made very, very restrictive and there's some problems with that. But, anyway, all I want to say at the moment is that Lenalidomide was used in experiment on immunosenescence, a very good experiment conducted at UC San Francisco. And it succeeded in improving the immune strength of the participants in various ways.

I'm not sure if it was exactly the NK cytotoxicity. I’m sure it was involved, but I don't have that data. And it also very happily, it inhibited some of the cytokine issues that we are looking to drugs like Rituximab for. So you have sort of a double barreled possibility here. Now you have a lot of business and political problems with this drug that I will perhaps write a memo to the FDA offices on because I don't want to bore you all. But I think that this is a very, very promising drug. I would love to get my hands on in much smaller doses than is given to cancer patients.

Finally, the last thing I want to mention is that I have had palliatives given to me in the earlier stages when I was not so ill. And I think there are a long list of palliatives such as drugs that are helpful to Dopamine, helpful to Norepinephrine, these sorts of things can help people function a bit better while they're in the milder stages.

Anyway I think that's enough for the time being and I want to say how pleased I am that FDA is getting on this. And I have now had this disease for 23 years and I have wondered if I would ever have a well day before I died. And I am greatly encouraged by the FDA and by other efforts that are going on. Thank you.

Dr. Sandra Kweder: Well, thank you so much Mrs. Waroff for your comments. I loved your comment about making salad and making guacamole because that is exactly the kind of thing we need to figure out, you know, what that equates to in other patients so that we have a common language and a common way of capturing that in the clinical trials because obviously - and I would be the same way. Like if I could - if a drug made a difference for me whether I could cook dinner or not, that's a big deal -- that is a big deal.

Deborah Waroff: Yes.

Dr. Sandra Kweder: And our challenge is to take that experience that patient's have and find a way to ask other patients what their equivalents are and capture that. So thank you so much.

Deborah Waroff: Thank you.

Coordinator: Thank you. The next is from Victoria Bell. Your line is open.

Victoria Bell: Good morning, thank you. My name is Victoria Bell and I've had ME for 24 years. And I have several questions this morning. First of all, I would like to thank Deborah for mentioning that making salads can be a marker of improvement.

I have had that experience once in my 24 years where I was able to make salads again for a brief period of time. So I would like to thank you for bringing that up and also for Dr. Kweder's conversation about that.

This morning, I'm particularly interested in medication that has been available and was covered under insurance until Part D was implemented and that is Klonopin. That is the brand name. The generic is Clonazepam. Klonopin helps many, many thousands of patients with this illness. For me, if I help my brain, then I help my massive cardiac symptoms.

And what happened when Part D was implemented was I no longer had insurance for it because it is the brand. I do not tolerate the generic and a lot of patients don't tolerate the generic. It cost $3000 a year and, since I am disabled and on disability, it's an extreme hardship for me to obtain the amount that I need. In the past several years I have had to cut back and choose between paying my bills, buying food, or being able to have Klonopin.

And I have had to cut back from my effective dose of Klonopin just in order to have some benefit from it. And I'm - so my question here to you, is there anything that the FDA can do to make Klonopin brand available under Part D for those of us who specifically need it?

I understood in the early days of Part D when I was advocating and calling all kinds of places, congressman and the AIP and there was an organization in

New York who was working on this that part of the reason that Klonopin was removed and Benzodiazepine the class - actually I'd like to interject here that the two classes of drugs that have helped me the most - most drugs I don't tolerate. But the two classes that helped me the most, Benzodiazepines and I can't think now of the class that Phenobarbital is in?

Woman: Barbiturates.

Victoria Bell: Those two classes were specifically removed from Part D and I do understand that a number of people in our society, young people and people in particular like Stevie Nicks who has really bad things to say about Klonopin.

They have used these drugs for the wrong - not medically approved reasons. And I do think that Klonopin should be available for people who, number one, it is not addicting; number two, I have been using it for 12 years. I can vary the dose hour by hour, day by day significantly. For instance, when I go see my specialist and I must travel by air and I'm by myself and I'm subject to all the sounds and activities of travel. I can increase that to 8 or 10 milligrams that day when my normal dose may be 3 milligrams and then drop back the next day once I'm out of that overly stimulated environment. So my first question here, is there a role that FDA can play in making this drug available under Part D to those of us who desperately need it?

Dr. Sandra Kweder: You know what, I'm going to - there's a couple of things here. I know that Dr. Michele knows a fair bit about this whole business of Part D. One thing, as a practical matter that I don't know if you've looked at and you may have already done this, but there is - there are probably several generic companies that make a generic. And usually when patients can't tolerate a generic, it has something to do with, you know, one of the things that, you know, holds the drug together is an inactive ingredient in the particular generic.

Victoria Bell: Yes, thank you for bringing that up because that was sort of a subdivision that I was going to get to.

Dr. Sandra Kweder: Right, right. And they're not really best ingredient, but I would urge you to keep your eyes open and work with your pharmacist to identify if there are other sources of the generic. You know, other companies that make it because those may differ from one - even though the active ingredient is the same, they may differ from one company to the other. And I had great success with patients in helping them identify a generic that, you know, sometimes it's just - you know, everybody's a little bit different. And it's what we call an excipient that they're bothered by.

Victoria Bell: Yes.

Dr. Sandra Kweder: And those change over time. Different companies come in and come and go from the generic market. I'm going to turn this over to Dr. Michele.

Dr. Theresa Michele: Hi, so first off thank you for your comment. I think you bring up important aspect issues for patients with chronic fatigue syndrome. And one of the roles of the Chronic Fatigue Syndrome Advisory Committee is to try to address some of those agencies across agencies. And the agency at HHS that deals with these kinds of issues is the Centers for Medicaid and Medicare Research and I can tell you that the upcoming Chronic Fatigue Syndrome Advisory Committee meeting, there will be a specific session by the Centers for Medicaid and Medicare Research. So I would suggest the - if you go to the CFSAC Web site on HHS, so if you just go to hhs.gov and type in CFSAC the, website will come up.

Victoria Bell: Right.

Dr. Theresa Michele: And just this week they opened the registration for that meeting and also the registration for open public comment. So I would urge you to register to give comments such as these to the CFSAC so that they can be addressed.

Dr. Sandra Kweder: Can she do that by phone?

Dr. Theresa Michele: Yes, you can do that by phone.

Victoria Bell: Thank you very much. I did go there. I do receive the emails and I did look at that yesterday. So thank you very much for this information because I will do that now that I know what part of the agenda will be.

Dr. Theresa Michele: Yes, the agenda should be coming out soon and nothing at this point is finalized, but I think it would be worth addressing your comments to the committee.

Victoria Bell: All right, thank you very much.

Dr. Janet Woodcock: Hi, this is Janet Woodcock. I joined the call.

Dr. Sandra Kweder: Okay, hi Janet. I wanted to do a time check here. Operator, we have 12 people waiting to ask questions and about 45 minutes. So just to let everybody know that we have - we are thrilled that there are a lot of people who have questions, so let's continue on.

Victoria Bell: Oh can I - I have one more question.

Dr. Sandra Kweder: Sure.

Victoria Bell: May I just ask this really quickly? A number of us are wondering if in individual patients, I don't belong to an organization. In developing the treatment option I noticed that - so I put on my notes here you indicated that some of the stakeholders involved in the development of this would be clinicians and we're wondering how - sort of what the criteria you will be using to select clinicians.

It is hoped that you would select clinicians who have several decades of experience before we lose their knowledge base. You know, most of them are aging along with our population, those of us who have been ill for decades ourselves, and there's just a fountain of knowledge available from clinicians like Nancy Klimas, Paul Cheney, David Bell, Dan Peterson and Dr. (Zabloshian), (Demueller) and Derek Enlander.

So, and I'm sure other patients have doctors - some of our experts that they can contribute to the wealth of resource that you might draw on. But so the question is what are - how will you be selecting clinicians?

Dr. Sandra Kweder: Well, I'm glad you asked that question. Thank you. Some of those names that you mentioned are very familiar to us and we will be - we're looking for people who have clinical - have long-term clinical experience or just have a long standing interest in this condition.

And we are wide open to suggestions from folks in the community if you want to submit those names to us over our Web site, there's a way to contact us. We'd be happy to follow up on that and follow up ourselves. So thank you.

Coordinator: Thank you. The next is from Danielle Patient. Your line is open.

Danielle Patient: Oh hello, I'm going to get right to the point. The FDA has a credibility issue and number one we need to get a sense of urgency from you. We've heard it in words. Now for the FDA to really rally the patient community and the research community, you urgently need to approve something soon. I can't emphasize enough the symbolic importance of putting a sign out there to the world this is a serious illness and the only way you will do that is with action.

Number two, I'll try and get through this quickly. Part of the understanding of the severity of ME needs to go into your analysis of side effects of drugs. We've heard many people say that drugs such as Rituxin should not be repurposed for ME because ME is benign and risk to benefit ratio that you talked about earlier.

If you do not understand the risk of the disease in the first place, you won't understand the willingness of patients such as me who have only had ME for 15 years and I say that sarcastically. Our willingness to jump at an opportunity like this, to seize part of our lives back for ourselves and our families and our loved ones.

I wanted to talk very briefly about measurements and emphasize how important measurement is if you do not link it with which definition of ME and I will add the CFS for your benefit - which definition you are using. If you do not identify that, then your measurements will continue to be all over the map as is the case in research.

So, just a few examples of measurements and measurement issues that you should consider. I recently had a VO2 Max test, retest protocol and for someone like me, just the process of travelling down, I'm travelling down to the area where I was getting the VO2 Max testing. That already put me into post-exertional neuroimmune collapse. So the differential between the first

test and the second test was not dramatic, however my anaerobic threshold is at 93 beats per minute.

So right now, I am in anaerobic metabolism. Talking, walking, basic things like that. So one measure, get it on your radar screen, is the anaerobic threshold and where as we have heard a lot about the differential between VO2 Test 1 and Test 2, if a patient is severe enough they are already collapsed by the time they get in for the first test.

So people like Dr. Peterson talked about NK cell dysfunction minus 3 and he uses that - I've heard him say that that is his number one measure of function. I would also add that things like the FitBit, there's technology such as a FitBit, it's essentially actimetry that also measures sleep that has an automatic download to the internet.

Technology such as the body BodyBugg or the FitBit are ways that you can actually physically measure the activity of the patient before and after treatment. Another one, somebody had mentioned the salad. For me, if I'm doing better, I'm not just living on the main floor. My bed is not on the main floor and I'm able to do one or more flights of stairs in a day.

So again just coming back, if you're going to show your sense of urgency, look at things like repurposing Rituxin, approving Ampligen, getting it done quickly because until then it's just talk and we've had talk for decades. And I do firstly want to say I appreciate the effort. I think this is more than we've heard in a long time, but your credibility issue is very real.

And you've talked about the FDA acting in a timely fashion. Now is the time to act. You need to get drugs approved for CFS. A few categories of drugs - I'm one of the very few people; I've had five different types of IVIG. My

number one favorite was actually in Germany and it completely obliterated my post-exertional malaise as well as my cardiac symptoms.

There is a huge body of research in the Women's Ischemia Syndrome Evaluation and you need to link with that because already just last year we have more research coming out in endothelial dysfunction.

So I'm going to close now because I know there are other people waiting. I'll email some more, but you need to get back to the issue of which definition are you using and that will draw which experts you should be listening to. And again categories of drugs, we need antihistamines for histamine tolerance. We need drugs for orthostatic intolerance. We need drugs for life threatening endothelial dysfunction which I've had.

We need nitrates, beta blockers, ACE inhibitors. And we don't just need drugs; we need medical devices, possibly Aethlon Medical Hemopurifier and again vaccines, blood and biologics. So I'm talking about IVIG. My number one was Pentaglobin which wiped out my post-exertional malaise for two to three months.

So, thank you again for your efforts and you need to match your intention with approval of a drug as quickly as possible. Thank you.

Dr. Sandra Kweder: Well, thank you. I'll respond very briefly to that and say, you know, we appreciate your recommendations on measurements to consider. And going in reverse order, we absolutely do understand that patients with serious conditions are willing to accept more in the way of risk.

And that is really one of the fundamental precepts of all of our expedited programs such as accelerated approval and expanded access of drugs under

investigation. That is a promise of the program that patients with serious conditions are willing to accept more risk than patients with conditions that are not serious. So you can be assured on that.

With regard to our credibility at approving something, this really gets back to the heart of what is FDA's usual role. We can only approve drugs where we have an application that is submitted to us for approval. That's the law. We can't just pull up a drug and say, "We think this works and we're going to go ahead and approve it." We need data and today the only application we have seen seeking approval for either ME or CFS is Ampligen.

And as many of you know we'll be holding an advisory committee to review that application in December of this year. So we can't go into any specifics. We're not allowed to do that because it's under review right now. But there will be a public advisory committee meeting in December of this year to bring experts to the table to discuss that.

So next caller, please. Thank you.

Coordinator: Thank you. If you have a question, press star 1. Please limit your comments to three or four minutes so we can get through as many in the list as possible.

The next is from Justin Reilly. Your line is now open.

Justin Reilly: Thank you. Can you hear me?

Dr. Sandra Kweder: Yes.

Justin Reilly: Okay yes - okay first I have some comments from my father who's an FDA lawyer. Sorry I wanted to turn my speaker off. Okay he was a former FDA

lawyer among other things. He wasn't able to make the call. Unfortunately, he had a last minute meeting.

Now he says you don't have to say this is a serious disease, as you know, and that the government has had a lack of effort before historically. So we need to put maximum amount of effort behind it and make up for some lost time. And the main thing that he did for years at FDA was to try to get the vitamins limited on the market over the counter to 100% of RDA.

So he is a hard core FDA person in terms of making sure that any kind of supplements or medicines are safe and effective. You know he's not into these kind of frou-frou alternative treatments. So I'm just saying he has some credibility here and he's seriously now behind the effort to, you know, have FDA and the other federal agencies get a maximum effort behind it and make up for some lost time.

I'm going to add my own comments here also. Please use ME, not CFS. CDC has made up this term CFS and placed the historical WHO term of myalgic encephalomyelitis with this sort of weak term of CFS. And it's just really inappropriate.

Also, CDC has come up with some fake definitions like the Reeves definition and there are other fake definitions that have intentionally been used to inflate chronic fatigue syndrome or ME with idiopathic chronic fatigue.

So, I heard someone from the FDA talk about, oh well, we need biomarkers; we need measurements. So we're going to be looking at, you know, how your fatigue differs from other people's fatigue. Fatigue is one measure, okay so we'll look at that. But I want people to really realize that fatigue is only one aspect of this disease.

Dr. Sandra Kweder: Yes.

Justin Reilly: I'm sorry?

Dr. Sandra Kweder: Yes, we understand that.

Justin Reilly: Okay, yes. So like think about it in terms of MS or, you know, AIDS or something like that. You know, just don't focus on fatigue. And there are plenty of biomarkers out there. The studies have been small.

I think FDA needs to step into the bleach and really fund those studies to solidify those biomarkers because there's tons of them out there. Okay, I would say don't listen to CDC, anything that they have to say unless you have independent confirmation from actual experts. Those could be patients who are experts or clinicians or researchers who actually do have a bona fide interest and who have bona fide knowledge of this disease.

Now, yes, I would certainly say Rituximab, please get started on trials for that. That's extremely important. Of course look at Ampligen, do biomarker development. Use those current biomarkers I was mentioning.

And I'll limit it to that. So thank you and that was a number of things, but I would really hope that you would consider that. Oh, I'm a lawyer too and a bunch of the other people that haven't identified themselves of the professions - I've noted there's some Harvard graduates there, law professors. So through patient community, who's been around - I've had ME for 10 years. I'm one of the younger ones here who's involved. You know, the ones who have had this for decades have been studying this disease for decades. And so, they're more knowledgeable than most of the MD's out there. So I would say also please

listen to the patients, you know, the ones that demonstrate that they do have some knowledge of the condition.

And that's it. Thank you.

Dr. Sandra Kweder: Okay thank you very much. And I do recognize that there is a lot of controversy around terminology and definitions. We are listening to everyone. So thank you. Next.

Coordinator: The next is from Andreas Kogelnik. Your line is open.

Dr. Andreas Kogelnik: Yes. Hi, thank you. I'm actually a physician, but also have a number of people close to me with the disease. And I wanted to, A: thank you all for doing these talks. I think it's very critical to change the context of the conversation, as Bob Miller and several other folks on the call have already stood out.

And you all have pointed out the lack of biomarkers is critical, but I don't want to dwell on the scientific side because I think we're actually making some progress there and hopefully we'll get an opportunity to discuss those things with FDA shortly. But I did want to touch on the point that I think even the last caller touched on which is actually interagency communication within the government.

I think the CDC had started to turn towards a very different path than they've taken historically, so this call is welcome if the FDA is doing the same. But...

Dr. Sandra Kweder: Oh I'm sorry sir, we've lost you. You're fading out, doctor.

Dr. Andreas Kogelnik: It's a benefit everybody can have (unintelligible) and other corridors in the federal government to support this. A lot of what the comments have revolved around is sort of the chicken and egg problem.

The pharmaceuticals aren't going to get involved with those until there's more evidence. There's not too many anymore obviously until we have a better definition of the disease and so forth. So you're not going to get any trials proposed to the FDA until we have more salient markers.

So I just wanted that to be considered and, you know, I'm not sure CFSAC has traditionally really addressed that issue. I know there's a lot of people sitting at the table there, but I think that is one key factor coming from the community that we need to have that level of organization at the federal level because this is such a complex disease and is quite different in many ways than many other diseases. So thank you for that.

Dr. Sandra Kweder: Well thank you for your comments. We did miss a little bit, but I think we got the big picture there. And we agree that - you know, and we obviously know we can't do this alone -- we absolutely have to have our federal partner colleagues involved in this.

And it is one of the reasons that we are going to pull them in into that discussion at the meeting in spring. You know, some of those other agencies have an ability to fund things that we can't and we will be pressing them to do just that.

Dr. Michele, do you want to comment?

Dr. Theresa Michele: Yes, I'd also just like to comment that that's really - part of the role of the CFSAC is to allow the Ex-Officio members to get together and do that crosstalk between the different agencies.

And there's also been a very high level committee started to jumpstart this within the agencies where they have people at the commissioner's level at FDA as well at similar levels of other agencies to really try to work on that intergovernmental communication. But we recognize that that has been an issue and we're really trying to move things forward so that we can leverage the expertise across the different agencies.

Dr. Sandra Kweder: Thank you. Next caller please.

Coordinator: The next is from Rivka Patient. Your line is open.

Rivka Patient: Hi, thank you so much for holding this meeting. I really appreciate the patients who helped to organize this and also the FDA officials. So, thank you.

Bob mentioned - Bob Miller mentioned there was an article today in the Scientific American about Dr. Jerome Horwitz and AZT and one quote from the article was, "Despite the risk, the FDA approved AZT at an unheard of, rapid pace. AZT became the first drug to treat HIV/AIDS." So I think that's a good thing to keep in mind.

I wanted to just give a human face to this illness as (Deborah's) taking the picture of making a salad did. I used to be a straight-A student, a mountain hiker, a global traveler working in Panama in the public health field. I was climbing the career ladder in international relations and then the next day I didn't have the strength to brush my teeth. And it's now two decades later and I'm still bedridden and homebound much of the time.

And many of us, the one to four million of us, feel abandoned by our government and the medical community that refuse to believe our illness is real and didn't the illness seriously in large part because of what Justin was talking about. The illness is labeled fatigue and that that in part and other reasons too allowed the media to make fun of us and ignore us. The NIH ignored us which, was devastating, but the CDC did worse.

They published studies saying that CFS was an inability to handle stress. It was due to childhood abuse or emotional imbalance or we have personality disorders. This really hurt us on a very tangible level and that's what we're up against. That's the history of our experience with the U.S. government and that's why you're hearing some of that passion here today.

And that's why we're so grateful that you're meeting with us. I'm still bedridden much of the time and I'm here to ask each of you personally on this call, the FDA officials, but especially somebody said that some drug companies are here, I'm here to ask those drug company reps to also please help us where there's one to four million of us. So we should be a good market for money.

We really have felt for decades abandoned by the government. Case in point, I had a good friend this past summer who killed himself. He was lovely. He was sweet, kind, giving man. He had been bedridden, homebound for 17 years and we were good support to each other. And he just couldn’t take it anymore. He committed suicide. He had lost hope.

So this meeting is the right trajectory that we're on and I want to thank Dr. Woodcock for allowing it to happen. Obviously, treatments are critical. I know that the FDA right now is considering Ampligen and we're waiting for

it. I think it's in February for FDA to come out and say whether or not they're approving it.

Now is the time -- really I cannot stress enough. I have a doctor who's on the front lines of this illness. Has hundreds of patients who can't get out of bed and who see him maybe once a year because they just can't get out of bed. And then they pay for the appointment and that they're much sicker. He is happy to use Ampligen, so he is eagerly waiting as are many, many patients for word on Ampligen.

Another thought about treatments is as (Deborah) mentioned GcMAF. I too did GcMAF and it doubled my natural killer cell function. I had to go to Europe to get it. That near killed me through the energy output.

A third drug I want to mention is called mDAPTA, M-D-A-P-T-A which is a third generation of peptide T made by Rapid Laboratories. A study was done back in 1993 that showed it helped ME/CFS patients and nothing has been done since then. So one question is how does a drug company express interest in joining the stakeholder meeting or asking FDA to be considered for accelerated approval?

But before you mention it, let me just mention my two other points which is in terms of measurement, cytokine panels are often used nowadays by smart rheumatologists and others and the CFS doctors to measure the efficacy of a drug. And for me, personally, it's not making salads, but it's my ability to walk up the stairs without having to stop and rest mid-stairs.

So my question to you is, when drug manufacturers don't step up to the plate and don't demonstrate that a drug works, who steps in to help the patients? That's my question as well as how does a drug company express interest in

joining a stakeholder meeting or asking FDA to be considered for accelerated approval? Thank you again, especially to Dr. Woodcock.

Dr. Sandra Kweder: I'll see if I can respond to your comments quickly. Thank you so much for your comment.

With regard to how does the company step in to look at things like accelerated approval, you know, one of the first things that I can suggest is our website which has a wealth of information for the industry about how to get in touch with FDA, how to work with us and have conversations even before they initiate studies of a drug to treat any condition.

We have a whole system of we call it pre-IND or preliminary discussions where we meet with the industry to have those discussions about what are they thinking, how are they going to approach this, what do we know that could help them. And that's - we're setting up right now a bigger initiative for communications with the company under new legislative requirements that we have to improve our communications with the industry. So that's one way.

Your second question was what to do when companies don't step in. And I think that we'll see to that is the reason that we are holding a webinar in November on how to build effective advocacy. Our experience is that patients do make a difference, but they make a difference when they find ways to come together to synergize their efforts to reach out to academia and to the industry and say that, "We are serious. We need your help and we're willing to do what we can to help you get the job done."

There are strategies for doing that. I urge you to sign up for that webinar. Some of you are involved in advocacy groups. Some of you have mentioned that you are not. I urge you to find one that you are comfortable with, but

please sign up for that webinar. It will be free and we do have people here at FDA who have been working with advocacy groups and patients for years and years and have a lot of experience that they can share.

Thank you for your comment. Let's go to the next caller.

Coordinator: Thank you. Again please limit your comments to three to four minutes so we may get through as many patients as possible.

The next is from Janelle Wiley. Your line is open.

Janelle Wiley: Hi, I'd also like to thank everyone for this conference. And I wanted to ask something that's already been asked, but I didn't hear the answer yet. So I wanted to ask it again.

In looking for measures of markers for clinical effectiveness, what patient selection process do you have in mind because there's lots of different inclusions that are actively being used? And, frankly, the use of conflicting criteria, some of which include patients which have various unrelated conditions that are not ME or CFS. This has hurt the progress of research. So, whatever is used, it would be important to use something that requires post-exertional relapse as described by Jason and for others at all.

Dr. Sandra Kweder: Well thank you for that comment and, you know, your questions are exactly our questions is what do we know about all the measures that have been used? How reliable are they? What do we understand about patients whom those measurements have been tested? What are their similarities and what are their differences?

Those are exactly the kinds of questions and discussions we intend to have at the stakeholder's scientific meeting in the spring. So thank you very much. You know, we don't pretend to have all the answers. That is why we're holding a meeting like that and we expect it'll only be a first check.

Next question please.

Coordinator: Thank you. The next is from Cort Johnson. Your line is open.

Cort Johnson: Thanks. Yes, my question kind of follows on the last question which is what if you have a measure like VO2 Max which has received - it's received some study and that really receives a lot of studies. I believe most of the results have been positive and clinicians and researchers, Dr. (Koldomit) and Dr. Peterson, Dr. Klimas, many physicians use this measure in their practice to track how well their patients are doing. But the research may not fit FDA standards. What do you do with something like that?

You know, we don't get a lot of funding. NIH gets $6 million of funding. I think you can't expect the (unintelligible) to meet the standards that other more established diseases get such as diabetes or any of these other fields. But the anecdotal evidence is pretty compelling. So how do you measure in the fact that we don't have the research? We don't have the research background that other diseases get.

And we can't get - you know, if we wait until that's present we're going to be talking about this in the next 20 years.

Dr. Sandra Kweder: You know, Mr. Johnson, we face this all the time for all kinds of conditions and one of the things we have learned is that when you sort of put

out a cause for experts to come together we often find that there's a lot more information available than any one person thought.

And when we face a situation like this we try to bring all the sources of information together and often times we are able to construct something that helps us have confidence in a particular measure. You know, we have an office here at the agency for rare diseases.

You know, this condition doesn't really fall under that, but we are able to do this kind of thing for conditions where there are only 300 people in the world with the disease and come up with something that we can measure and hang our hat on. It is different than measuring the conditions that millions of people have and for which there have billions of dollars in research.

But we are committed to doing it and we think that we're going to have some success in this condition as well. But the key is that a lot of the researchers in this to date have been out there on their own. They're clinicians who are following a series of patients for decades. And no one's really been able to tap into the kind of information that they have.

And we know that they've got things that can be useful, but they need people like us and the NIH that does have funding to help them put the package together and make it speak for everyone. That's our challenge and we have experience in this and we're going to use that experience and do the best we can because we don't want to be having these same conversations in 5 years, 10 years, 20 years. We want to be having more sophisticated discussions about how to refine things. But here we're just getting started and we're going to push the envelope. So thank you.

Next caller.

Coordinator: The next is from Kim McCleary. Your line is open.

Kim McCleary: Thank you. My name is Kim McCleary; I'm President and CEO of the CFIDS Association of America. And would like to thank the FDA staff for making this call possible and assembling so that we can begin this dialogue and also to the advocates who, you know, contacted Dr. Woodcock's office and ultimately were successful in bringing this call together.

I'm delighted today to hear the clear affirmation from FDA that ME/CFS is considered a serious and life threatening condition and hope that the pharmaceutical and biotech partners on the line will take that as a sign that they should ramp up their efforts to take advantage of the accelerated approval measures that can be utilized or applications under ME/CFS indications.

And, also the plans for the Endpoints meeting next spring. I've been talking to Dr. Michele about this and in late 1992 or early '93 one of the FDA advisory committees did convene a meeting on endpoints and obviously it's been 20 years since that happened. But I hope you'll go back to your archives because some of the measures that the patients have been describing today were eliminated in that session.

The use of exercise testing and actimeter testing as endpoints for measuring activity and improvement following treatment. And I know how important the consensus about endpoints is. I was able to attend the FasterCures Celebration of Science this weekend and then heard from Dr. Hamburg and Dr. Woodcock about how the consensus on endpoint measures has advanced therapies for HIV, cystic fibrosis, multiple sclerosis and other conditions that I think are good models for CFS.

My question is: there are as different people have brought up many different definitions of CFS being used and often the research uses a particular definition, but then they make some subtyping choices in their patient selection methods that would narrow the population of ME/CFS patients to an even smaller number.

And I wonder what the current guidelines at FDA are for this more targeted testing of therapies and when a population - when it's subtyped might fall under the orphan condition guidelines if they were say less than 200,000 people in the country that would meet a particular subtype definition, whether those extra incentives from manufacturers would then be available?

Dr. Sandra Kweder: That's a very interesting question and we certainly do see that, but a couple of things do come to my mind. We often use, you know, subtypes or subgroups of people in clinical trials to really try to identify, you know, smaller number of patients, the effect of a particular drug.

That's where, if I was to issue a guidance document for industry on enriched clinical trials, it's called Enrichment Guidelines, how to do those enriched clinical studies so that you get to expose less people for a shorter period of time to get your answer. So that is something that we think about a lot from multiple conditions and, you know, we're open to the idea that this may be one of them.

There is absolutely a trend in the industry to look at smaller populations of patients with orphan conditions before drugs are approved. Again whether or not it applies in these conditions you'd have to be able to articulate what that sub-population is. But I know that the agency, you know, our office of orphan products is open-minded and willing to have those conversations with groups that are interested in doing that.

So thank you and I really look forward to your participation at our meeting in the spring. Next.

Coordinator: The next is from (Matina Nicholson); your line is open.

Matina Nicholson: Hello, thank you for this meeting. My question is for everybody. Can we come up with clinical protocols in the methodology of the clinical study potentially?

And I know we have to work with the CDC in regards to the (unintelligible) definition, but I think that will help us in getting the appropriate effectiveness of the drug to have like a clinical profile, like (unintelligible) biomarkers and everything like that. That's a suggestion. And then secondly I don't (unintelligible).

Dr. Sandra Kweder: Two things. Yes we agree on a clinical protocol if that's what's needed. In order to have a clinical protocol you got to have some agreement on what you're going to measure in that protocol. That's our goal. So, absolutely.

And in regards to advisory committees, we do have standing advisory committees to address a variety of conditions. What we would usually do is, you know, in a condition like this that requires multiple experts from many, many different fields we will use the core of one particular advisory committee and supplement it with experts who bring the richness of the experience and expertise to that core committee.

So we will probably invite many of those people who we would be contemplating including our advisory committee or who will be on the

advisory committee for Ampligen applications and invite them to our workshop in the spring.

But thank you for the opportunity to clarify that. Next question.

Coordinator: The next is from Tamara Parsons; your line is open.

Tamara Parsons: Hi, thanks everybody for being here. I have ME and have to understand that listening and talking and running - I can't run. They're all the same to me in terms of energy depletion, so I hope I can get the question out.

I understand we're not debating the difference between ME and chronic fatigue syndrome, although I do think it needs to be addressed and separated at some point. I'm glad that I understand about needing biomedical studies before you can begin drug development. I'm wondering if you think the persuasive belief of medical community and the focus of their research such as cognitive behavioral therapy and graduated exercise therapy kind of showing us that they think it's just a psychological disease or disorder?

I'm wondering if you think that maybe that is what is hindering the biomedical studies or anybody jumping in there? I know that ME is - has a lot of testable things and again I'm sorry I'm losing my ability to speak, but I'll do my best. It's acute onset. There's testable neurological changes. The fused brain injuries is observed on a brain SPECT scan. There's testable sleep and muscle dysfunction, vascular and cardiac dysfunction, endocrine dysfunction and cardiac dysfunction.

Dr. Paul Cheney, even though he doesn't separate ME from CFS, I think is one of the leaders in knowing about that cardiac dysfunction that comes with ME. People have mentioned clots and circulating blood volume and low

natural killer cell counts. There are lots of testable things that people can do and so I'm just - I'm hoping we can come to a point of differentiating between ME and chronic fatigue.

Hoping that the biomedical companies can be convinced by presenting these studies from doctors like Bryon Hyde, Paul Cheney, Elizabeth Dowsett and patient advocates like Jodi Bassett. I hope that they will find reason to do some studies so the FDA can get to work on a drug that will help us all. Thank you.

Dr. Sandra Kweder: Well, I want to thank you so much for your comments. We really appreciate your input and I want to be able - our commitment to helping you and helping the patients who are not on this call and helping any future patients who suffer from this condition.

That's all the time we have right now for your specific questions. If you're a few people who didn't get to ask your questions, there is a FDA email that was sent to you yesterday with the background materials from this meeting. If you still have a comment or a question and you want to submit that and want to get it answered, please send us an email and we will do that.

It's part of the announcement about the docket. If you have just comments, submit them to the docket. The instructions for how to do that is also in the materials we sent to you.

We've got about one minute here and I want to ask Dr. Woodcock if you want to make any closing comments if you're still on the call.

She must not be still on the call.

Woman: She got disconnected.

Dr. Sandra Kweder: Okay, well I really want to thank everyone for taking the time to listen, to speak. We've heard - your input has been tremendously valuable to us.

I do urge you, if you want to really understand how to help in drug development, how to further interest from patients like yourself, please sign up for the Excellency in Advocacy workshop. It's going to be done over the web in November. I think you'll find enriching information and we really look forward to your participation in that.

In addition, the FDA advisory committee to review Ampligen is a public meeting. There will be the opportunity for public testimony to be heard at that conference in December. What are the dates (Terry)?

Dr. Theresa Michele: It's December 20. The FR notice for that has not yet posted.

Dr. Sandra Kweder: But it will be posted in the federal register. We'll make sure to put information about that on the ME/CFS website so that you can access it coming up. You'll be able to see who is on (unintelligible). You'll be able to read once they're posted shortly before the meeting. You'll be able to read the transcript documents for the meeting as well. That'll be put together by the company and but with the reviews by FDA.

So and again we look - we have not set a date yet for the workshop in the spring, but we look forward to your participation in that and for any of you who can to the CFSAC meeting coming up in October.

Thank you so much for your time and for your input. And this is the end of our call.

Coordinator: Thank you. This concludes today's conference. Thank you for joining. You may disconnect at this time.

END