PUBLIC WORKSHOP
ON PATIENT-FOCUSED DRUG DEVELOPMENT:
DEVELOPING AND SUBMITTING PROPOSED DRAFT GUIDANANCE RELATING TO PATIENT EXPERIENCE DATA

Conducted by the Food and Drug Administration

Monday, March 19, 2018

1:01 p.m.

10903 New Hampshire Avenue

Silver Spring, Maryland 20903

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C O N T E N T S

P R O C E E D I N G S

MS. VAIDYA: Hello everyone, good afternoon -- if everyone could take their seats, good afternoon everyone. My name is Pujita Vaidya and I'm in the Office of Strategic Programs in the Center for Drug Evaluation and Research.

I'd like to welcome everyone to our public meeting today on developing and submitting proposed Draft Guidance relating to patient experience data.

We're very happy to see such a great turnout. With many patient, patient advocates, researchers, folks from academia and medical product developers in the audience, and we have several folks on the web as well.

So FDA is having a workshop today to hear from you all which will help us in the development of FDA's guidance to support patient-focused drug development and implement requirements under the 21st Century Cures Act and PDUFA VI.

In our discussion today, we'll mainly focus on identifying areas where patient experience data might be particularly helpful to inform medical product

development and regulatory decision-making and how that can be shared with others.

We will also reflect on the range of opportunities for patient stakeholders and seek input from patient stakeholders on what questions will be most helpful for FDA to address in its forthcoming guidance that we'll all be talking about today.

I do want to mention that in addition to this workshop, a docket will remain open until May 18th, 2018 to which the public may submit general or detailed comments around the topics that we covered today during the Workshop.

We do have a full agenda for today's meeting so let me quickly go through what's in store for you all. Theresa Mullin, Associate Director for Strategic Initiatives in the CDER will get us started this afternoon with opening remarks.

After Theresa I will come back up to give a short presentation to introduce CDER's external resources webpage. We will then have two panels focus on considerations on specific topics.

The panel sessions will be as follows:

Session 1 will be opportunities for patient stakeholders and hearing from the FDA's perspectives so we will have our FDA panelists appear. This session will start off with two -- two presentations from our FDA colleagues.

After that we'll have a short break and then we'll have Session II which is opportunities for patient stakeholders hearing from their stakeholder's perspective.

Following Session II, we will have an audience facilitated discussion so that those in the audience can add to the discussion that we're having up here after Session II.

We'll have many people attending via web. Unfortunately, we will not be able to take comments or questions or address them in the meeting itself, but we encourage you to submit your comments to the public docket and we'll be actively looking through those.

Following the sessions, we will provide time for open public comment. If you wish to sign-up to speak during the open public comment period please do so at the registration table up front.

Participation is on a first-come, first-served basis and we have about 20 minutes allocated for open public comment so we'll be able to take up to maybe 10 speakers or so.

Before I get into some brief housekeeping items I would like our FDA panelists sitting over here to please introduce themselves.

MS. MULLIN: Hello, Theresa Mullin, the Associate Director for Strategic Initiatives in the Center for Drugs.

MS. MALONEY: Good afternoon, I'm Diane Maloney, Associate Director of Policy in the Center for Biologics.

MS. SIPES: I'm Grail Sipes, I'm the Director of the Office of Regulatory Policy in the Center for Drug Evaluation and Research.

MR. FLANAGAN: I'm Keith Flanagan with the Office of New Drugs in CDER.

MS. PAPADOPOULOS: Elektra Papadopoulos, with Clinical Outcome Assessment staff in the same office.

MS. VAIDYA: Thank you, so this kind of will be in an active listening mode throughout the day. For

some of the sessions they will be moving over as they are part of our Session I Panel as well. We'll have our active panelist here for each session come up when the time is -- when it's time for them.

So just a few brief housekeeping items -- this meeting is being transcribed and a live webcast is being recorded, both of which will be archived on our website. We will have a 15-minute break at around 3 o'clock after Session I.

Bathrooms are down the hallway in the lobby to the left and if you need the WIFI password, I think we had it up earlier -- it will come up again during the break or you could ask our folks in the lobby, they'll be able to hand that over to you.

With that I'd like to now invite Theresa Mullin to the podium.

MS. MULLIN: Thank you Pujita. You know if you knew about this meeting and you've come here today, you may not need any orientation to what I'm going to tell you. I'm think I'm going to tell you maybe something you're very well familiar with but I am -- just in case you're not.

I'm going to give you a little bit of orientation to this guidance. We have a very long name that we use for it which is pulled out of the statute, but at FDA we've been referring to it for some time as Guidance 5. So why are we doing Guidance 5?

And so this session today is really intended to give you a better sense of the statutory requirements that we're trying to meet here and -- and let's begin with -- and this is a -- let me know if that's just too loud and I'm hurting your ears, but this is really to implement a section -- a paragraph under Section 3002 of 21st Century Cures.

And under Section Title III which is Patient-Focused Drug Development, we have to refer back to Section 3001 which starts out by talking about patient experience data.

And the statute defines patient experience data but it also begins by saying, "Directing FDA, that following the approval of an application, any application approved after approximately June of 2017 should make a brief public statement about a patient experience data and related information, if any, that

was submitted as part of that application and was reviewed as part of that application."

And so FDA actually to -- to get ready for that we put together a little template that in consultation with our reviewers to identify various types of patient experience data that we had been seeing and might see, and we looked at our benefit risk framework and the components, the five areas of consideration there to just give us a -- a kind of data collection template.

Because under Section 3004 of Title III, we have to begin reporting on that use of patient experience data in 2021 -- so that's a few years away, we don't want to go back. We want to start collecting that information going forward so that's the approach we've been taking with every application and then to prepare ourselves for later reporting.

Well what -- what is patient experience data and how is this defined -- and again you probably are all very familiar with this but just to go over it. It's defined in the statute as data being collected by any person and it gives examples including patients,

family members, caregivers of patients, patient advocacy organizations, disease research foundations, researchers, drug manufacturers as examples that are intended to provide information about patients' experiences with the disease or condition and in particular, the impact -- physical and psychosocial of that disease or condition, or regarded therapy or as amended under FDARA, clinical investigations and also patient preferences with respect to treatment of such disease or condition.

So when we talk about it in short hand today we might say patient advocacy group, we might say a patient is still part of their group, but think of all these groups that are named here as the longer list that we're referring to -- we just can't keep repeating that. You'll get tired of it and we'll never get through the meeting. So that's who we're talking about.

And now under 3002 there's a -- there are 8 paragraphs that are describing guidance that the Secretary should issue over the next 5 years and -- and our goal is to -- to issue this guidance, not to string

it out over the, you know, 5 years, but we will be doing it more or less in the timeframes and the cadence that we had described in FDARA commitments under Title I PDUFA VI, but these are -- are provisions in 21st Century Cures track really well and align with -- really compliment what we committed to under PDUFA and so that makes things really much better for us and it helps.

So this first area under 3002 is -- methodological approaches for how to collect patient experience data and submit that for regulatory decision-making so that it's accurate and representative of the intended population.

And these methods are collecting new meaningful patient input throughout drug development and considerations for data collection reporting and analysis. So that's a pretty broad remit but that's what we're trying to do under our first guidance.

And the second guidance area to address would be methodological issues for how to develop and identify what's most important to patients in terms of the burden of disease, burden of treatment, benefits

and risks.

The third area of focus is identifying and developing methods to measure impacts that are -- to patients that are most meaningful and also would be facilitated in collection of clinical trials. The remedies you are now focusing on the subset of impacts that really would be measurable and impacted by a -- a therapy or a technology that's being studied in a trial.

Not all impacts that patients identified may be affected by such treatments. And then the statute goes on and the fourth area here is methodologies, standards and technologies to collect and analyze clinical outcome assessments for the purposes of regulatory decision-making. So that's that broader set of types of tools, the previous few might really in many cases suggest a PRO but here, more broadly, we're looking at COAs of which PRO is a subset.

And then here we are paragraph 5 -- how a person seeking to develop and submit the post draft guidance related to patient -- relating to patient experience data for consideration by the Secretary may

submit such proposed draft guidance to the Secretary -- so that's the focus of the meeting today.

And as you can see it just is a fairly -- it's -- it's one of perhaps a number of different ways that information could be submitted. So in trying to -- to planning for this meeting today, we're trying to balance, not excluding or saying this is the only way to do it, but trying to talk about all the ways and when this guidance submission may be particularly appropriate or one that you might prefer to try using.

Paragraph 6 gets into the specifications of the format and content for a submission to the Secretary that would be including this kind of information and how we would intend to respond to those submissions and the timeframes, if it's not part of a regulatory submission that already has a timeframe.

And finally, paragraph 8 here, how the Secretary, if appropriate, anticipates using this information in its benefit risk assessment framework that was described elsewhere in the statute.

And so these are all the areas that we will be covering and those first four as I said, really align

pretty nicely with the first four areas of guidance development that we had identified as a commitment under PDUFA VI which is included in FDARA reauthorization last summer.

But in addition to that we have planned workshops that we will be conducting in each of those four guidance areas. And so we first thought we'd be having -- issuing a guidance, by now on this Guidance 5 but we thought better of it -- we thought really you would benefit for having a kind of discussion like this -- having a workshop first because we really get a lot of helpful input.

We'd get more insight about what's useful by hearing from our stakeholders and having discussions like this. So instead of having a guidance produced now, we're having this workshop so we can get that information in and we'll produce the guidance -- draft guidance later this year.

In addition, in PDUFA VI we're going to have MAPPs -- developing MAPPs and SOPPs to try to further integrate this kind of data collection in our regulatory processes internally in our own internal

review processes. We are committed to develop a repository of information that we'd make publicly available on the tools that are publicly available and other information that might be submitted to us and Pujita is going to say a little bit more about our initial efforts there.

We're committed to conduct a workshop where we'll really hear more about patients' experiences with clinical trial participation and get the recommendations of patients, caregivers, and others in the community about ways to enhance participation of patients in clinical trials.

And finally, we committed to increase our staff because we have rather limited staffing with expertise in the review of these kind of submissions and COAs and clearly, if people are going to want advice, or want us to do timely review, we need enough capacity to do it.

I'm not going to go through these in detail -- this is just a more lay version of what are we doing in each of these four guidances that are related to methodology -- related to PR roles and COAs and patient

experience data as it's called by the -- named by the statute.

We've also been asked, how do these guidances really apply and I think that you can consider these four guidances to really track very well with those first four paragraphs in 3002.

And we see the first two of these guidances really -- including the Glossary of Terms that we've included under PDUFA VI in the first guidance to be applicable throughout the lifecycle of a drug and really encourage that people think about applying and collecting and thinking about bringing in this kind of information as early as possible.

If identifying the disease and treatment burdens and outcomes that might be appropriate to address really would affect design issues and may affect the instruments you need to develop and have ready when you're ready for clinical trials, and so those are the things that begin to be addressed in Guidances 1 and 2.

Guidance 3 and 4 really become particularly important to apply by pre-clinical development

anticipating clinical trials and all the way through to post-approval studies, but it also is somewhat relevant in those earliest stages, so, -- so we think these guidances will have broad applicability.

This is not readable but it's taken from the back of our plan for issuance of guidance that we published last summer and it's available, yes on our website. You can Google "Applying for Issuance of Patient Focused Guidance," or things like that and the link is also there.

And this shows you the timing that we've kind of aligned our FDARA commitments to the 21st Century Cures timelines and there you have what we're doing. Only with the amendment that as I mentioned on this Guidance 5 -- we're having a workshop right now to get input and we'll have that post-draft guidance produced a little bit later this year.

Here's an update on where we are with the work related to these things. We had that first workshop on Guidance 1 -- Collecting Comprehensive and Representative Input last December, and there's a link to the discussion draft that we produced in advance of

that meeting and we are planning targeting having our draft guidance on number 1 in by June or in June -- depending on the clearance process.

And we have launched a website for externally submitted information related to patient experience data and Pujita can tell you more about that. We felt the need to have something ready because we're receiving a lot of very helpful information from external groups and we want to be able to share it, so this is the way we put this together so we can begin sharing that without any more delay there.

And today's workshop is to help us with -- you can see why we call it Guidance 5 because there is the title of it, "Developing and Submitting Proposed Guidance Related to Patient Experience Data for FDA Consideration."

And so with that I'll turn it over to Pujita.

MS. VAIDYA: Thank you Theresa. I apologize if I start coughing -- my allergies have kicked in so please bear with me. So now as Theresa mentioned I'll be going over our new external resources page that we've -- we've just recently put out.

Things I will be covering at a high level here -- What is patient experience data -- I probably won't go over that since Theresa has talked about that. Give an overview of our CDER external resource webpage -- then kind of go into a little bit of detail about some of the categories of external resources that we've included as of now and some additional resources that we have available for everyone.

So just frequently asked questions, cover page guidelines and stuff like that.

Okay, so as Theresa's mentioned in her opening remarks in 21st Century Cures Act, we were introduced -- formally introduced to the term "patient experience data" and we'll walk through this because we -- I think by now we know what patient experience data -- or as they call it, PED, actually is.

We recognize that there are various types of patient experience data. It can be collected in many ways and we've seen different work products coming out of this so let's say for example meeting reports capturing the patient's perspective or proposed draft guidance is what we'll be talking about today.

And as Theresa mentioned in her opening remarks, we heard from our patient stakeholders that there really was a need for a centralized location to house these types of information and to not only to house it, but to share it with folks so they can serve as a resource for not just us, but for all of our stakeholders.

So keeping that in mind in January of 2018 CDER launched its external resources or information related to patient's experiences webpage. This is a pilot webpage and this is intended to be a platform to help facilitate public discussion on a patient focused drug development.

What we have here on this webpage of certain links -- publicly available links that are either excellent reports or other resources and information. We see these resources serving as a resource for all of the stakeholders, for patient groups out there, patients themselves, the researchers, drug developers, mobile product developers and federal agencies as well -- like FDA.

Anyone can submit this information and -- but

we would like to note that although FDA reviews the materials that are housed on these specific links so when we do get a request we do go in and review the materials just to make sure that they are in within the scope of the webpage itself.

We, however, do not assess their scientific merits or compliance with regulatory requirements. Please also understand that FDA's decision to post links to the materials does not necessarily reflect an endorsement of the authors, responses, or the content itself.

So now I'll talk a little bit about the various categories that we have so far on our webpage. Currently we have three focus areas -- x-ray, led PFDD meeting reports or other stakeholder meeting reports -- that's the first one.

So what do we mean by that? So in this category we -- we plan to include meeting reports from x-ray led PFDD meetings -- the types of meetings that several of you in the audience are conducting or have already conducted. It's in the reports that are generated from that. Along with that we also -- we'll

be housing other stakeholder meeting reports where you have kind of a list of the patient's perspective on disease burden and disease areas. So that's what we plan to put in this category.

The next we have here are proposed draft guidance relating to patient experience data -- the topic of conversation today. So here external -- external stakeholders may submit links to publicly available proposed draft guidances and we were looking to including that on our website.

I would like to note though there is also an existing procedure for submissions of external guidances which are provided under -- this is a lot of jargon -- 21 CFR 10.11 F3. If you have any questions come find me and I can talk to you a little bit more about that.

But that's the formal process but here itself I would say if you'd like it on the website we ask that you submit it here as well.

Finally, the third category we have so far is Natural History Studies or Other Disease Specific Background on Condition and Discussion of Unmet Medical

Need.

So in the case of let's say -- natural history studies we understand that that can be retrospective, prospective where survey studies are conducted. And if they are published on a website and are publicly available you may submit those website links to us.

You may also provide links to other publicly available reports or other documents providing disease-specific background on a condition and unmet medical need.

As I mentioned earlier this is a pilot effort so as we receive submissions, categories may be added, revised or deleted as needed.

Now I'll go over some of our additional resources that we have available for -- for folks. We have our frequently asked questions document which is on our website and it is really to provide a little bit more information on the scope and the process overall.

Some high-level questions here -- there's more in the actual document. What is patient experience data? Who can provide these publicly available website links that we're talking about? What types of the

resources will be included on the page? So what's in scope and what may be out of scope here for this particular web page that we have.

And we'll go over the process -- over our process of how can you submit a publicly available link to us? So with that and in keeping that in mind the last question -- how can you submit a publicly available link?

Well, we have a PFDD resources email -- email where we ask you to submit your resource itself. But along with that we ask that you include a cover page as part of your report or the resource that you are submitting containing the information to provide a little bit more -- greater transparency.

The cover page may be included within the report of the resource that you're submitting to us so it could be -- if it's a report it could be a first or second page itself or it can be housed on the same website link as your actual resource.

So if you have a report on a page you can have the cover page as a second link there so that it is both in the same place.

Some things that we ask that you include on -- in your cover page -- the title of the resource, authors or collaborators -- so if you've worked with consultants or other scientific writers, we ask that you disclose that.

Funding -- funding received or granted, if any. And if you have not received any funding we ask that you include a brief statement on that as well. Diversion date -- please include a statement that the resource has not been revised or modified after the time it has been shared with the FDA and also a statement that the resource can be linked from our website -- FDA website, so just giving us permission to link to your page, that's very important to us.

So just -- these are some high-level steps. I talked about the web page itself, some categories, some additional resources we have. If you have other questions please feel free to reach out to us and email us. This is a pilot so as we are modifying -- as we go through and issue this we'll modify the webpage and the process as we go. If you have any feedback please do let us know.

If you see that something's missing or just general feedback on how we're communicating this please let us know. If you have a resource -- I don't think I showed the email address. We have PFDDresource@fda.hhs.gov. For more information we have CDER's patient focused home page and then our patient focused email log so a lot of folks are probably already with but just feel free to email us.

And then with that, thank you all and I will now slowly move us into Session I discussions for today. So for Session I we're going to be talking about Opportunities for Patient Stakeholders and hearing the FDA's perspective.

Our moderator for Session I will be Sara Eggers so I'll ask Sara Eggers and our panelists for Session I to please come up and take their seats, thank you.

MS. EGGERS: Good afternoon, it's a pleasure to be here moderating this session today. The session is -- this first session is seeking to gain FDA's perspective on opportunities for patient stakeholders to develop information related to patient experience

that would provide helpful data and information to support patient focused drug development in a specific disease area.

In some cases, this work product could be well suited for submission as a proposed draft guidance. In other cases, it may be more appropriate or more helpful submitting other forms of work products and we are going to get into that today.

We'll first discuss what patient experience data may be particularly helpful to inform medical product development and regulatory decision-making broadly.

Again, we'll be getting FDA's perspective on the types of information on patient experience data to collect and measure and talking about various formats for effectively sharing that information.

There are two important presentations -- helpful presentations, I found them helpful that we will have first. Theresa Mullin will come up first and present on the range of opportunities that external stakeholders have to contribute to their expertise and information regarding patient experience.

And then Keith Flanagan will come up and give a very helpful primer on guidance and the guidance -- and guidance development. And then after those two presentations I'll come back up and we will engage our panelists. Can we first before the first speak, can we have everyone go through and introduce yourself on the panel?

MS. LAPTEVA: Hello, my name is Larissa Lapteva and I'm the Associate Director in the Division of Clinical Evaluation, Pharmacology and Toxicology in the Office of Tissues and Advanced Therapies in the Center for Biologics Evaluation and Research.

MS. LOWY: Hi, I have a shorter title. I'm Naomi Lowy, I'm Associate Director for Regulatory Science in the Office of Drug Evaluation I.

MS. MCCUNE: Hi, I'm Susan McCune and I'm the Director of the Office of Pediatric Therapeutics in the Office of the Commissioner.

MS. MULDOWNEY: My name is Laurie Muldowney and I'm the Associate Director for Medical Policy in the Office of Translational Science.

MS. MULLIN: Theresa Mullin, CDER.

MS. PAPADOPOULOS: Elektra Papadopoulos, Clinical Outcome Assessments Staff.

MR. UNGER: I'm Ellis Unger, I'm Director of Office of Drug Evaluation I in the Office of New Drugs in CDER.

MS. EGGERS: Thank you very much and now if Theresa could come back up.

MS. MULLIN: Thanks Sara. So again, I alluded to this a little bit before and we're having this workshop today and you look at all these provisions in Section 3002 and all the kinds of guidance we're going to be providing about how to collect information and how to submit and there are many opportunities.

And what we struggled with a little bit when we think about guidance is that guidance to industry -- we do guidance for industry, has a much narrow purpose and so we thought that we wanted to have a discussion around all the ways that the patient community and stakeholders that are interested in developing patient experience data could contribute and not have people take away the message that it's just guidance.

The only thing that's useful to submit to FDA

is guidance -- that's the last thing we would want you to think because there are so many other opportunities and many that may really serve as a better vehicle for the kind of information that you could provide.

So, so first of all just an observation that in parallel with our expanded efforts in this we're trying to ramp up in our efforts here in patient focused drug development.

We know we've heard from a number of -- of patient and disease advocacy groups and others and companies too that they substantially are trying to increase their own efforts in this area.

And a number have asked us how can they help -- and what can they do? Sometimes those groups are even led by regulated industry or supported by industry or they're supported by, you know, patient's resources and other sources of funding, but they want to know how they can help and we think there's a lot of help that's needed so we're trying to come up with an overview of what might be -- not exhaustive, but just ideas of the kind of things that occur to us that could be helpful.

And it might really depend how they contribute

-- probably depends on your expertise and your perspective and where your own relative strengths lie as an organization or as a collective -- a collaborative of organizations.

But for example, we note that groups have typically got access and expertise in the -- access to patients and expertise in what patients are living with when they're living with their disease or people who are caring for patients with a disease.

They also -- they have especially good access to clinical disease experts -- people who perhaps have experience doing trials and knowing what it's like to enroll people with that disease in trials and the issues that they may face. They may have good access and you may have that as part of your collaborative academic experts who have a great depth of knowledge in that disease area.

Drug developers who have particular interest in that disease as a target for development of drugs and generally we find that many external groups have great communications and outreach expertise which -- you know FDA's trying to build its bench there but

we're always sometimes described as a culture of introverts so we may not necessarily have the same strengths that you all may in those areas.

And honestly, we're just aware of other things -- other patient access related issues, whether it's access to trials or access to therapies that are approved and other issues that you know about or can help flag and -- and provide insight about.

So here are some of the areas -- I'm going to name a number of areas I'm going to talk a little bit more about a few of them that have been identified in discussing this with my leadership, also just helping to contribute to this list from -- from the perspective of the Senate Director and the Senate for Drugs as well.

But the first and the most -- maybe the earliest way that groups have contributed is by gaining additional support for research in a given disease area and this is through advocating for increased funding, making those who have funding aware of the need.

And I mentioned in a meeting that -- it was Patients as Partners meeting that was held last Friday

that maybe in addition to basic research which has long been one targeted area of need for research, there's probably a lot of applied research that's needed -- questions that are related to a particular disease area and understanding the experience of patient's -- patient's experienced data is another type of research opportunity.

You can also help people with the disease for example providing and making sure that they have access to the durable medical equipment like wheelchairs that they may need as their disease progresses.

Outside groups are particularly well-positioned sometimes to develop natural history studies and these can be extremely helpful -- not only to inform future research and the design of that research, but also as a basis for recruiting patients into those studies so that patients in a given disease area are clinical trial ready and that just helps with development expediting development of drugs.

Some groups have also formed patients' Centers of Excellence. If you have the resources and experience that gets built over time there was a

presentation I heard last week by the Addario Lung Cancer Association, David LeDuc described his Association's work with others in California and in the west to develop Centers of Excellence for treatment of lung cancer.

It was very impressive to hear about their journey over several years but this is something that might be within your reach depending on your interest and your resources.

Also, venture philanthropy may be helpful focused on a given disease area where groups who are watching that area can see that certain products in the pipeline are really looking like winners and you help expedite development to get them over the finish line.

Here are some other areas that may be just closer to the ones we often talk about here in relationship to FDA and the first has participation in our policy development and responding and giving us your input to our meetings and workshops and also with your request comments.

Coordination of work among the patient advocacy groups, communication and education and

outreach and that's a variety of things -- I'll say more about that in a minute, convening meetings and workshops that could be done and really address more quickly and in more detail, needs that are out there that FDA may not have the bandwidth to get to or we're not getting to as rapidly as you may want to or be able to do.

And in addition, you -- groups can contribute to guidance development and they can submit new or enhancements to existing guidance. So in terms of participating in our guidance and policy development -- we're -- we're planning a lot of meetings, as you may know.

In fact, you might know if you want to get a parking pass here or something we should look into that, you know, actually FDA employees have a hard enough time finding parking -- I shouldn't say that.

But we are going to have and we have been having a lot of meetings related to patient focused drug development issues. And these meetings -- there's just no doubt that the meetings are not really anywhere near as good if we don't have the inclusion of the

patients and people in the community -- it makes the meetings the most -- provide the most insight for us and the most valuable if we get strong participation.

And external groups are really important to help us get participation of people in their community and that includes all those groups I mentioned earlier that have access -- they have access to. They can help us get rich participation in these meetings. They could also help us identify issues up front that we ought to be addressing in these meetings and in making sure that we are really increasing the value and maximizing what we learned in these -- our meetings, so it’s an opportunity.

We also see an opportunity for helping coordinate across groups. If there are more than one advocacy group or more than one stakeholder group in a given disease area sometimes groups don’t know what others are doing, they have limited resources. It would be really great to minimize the you know, duplication of efforts that unintended duplication or conflicting work that might be going on by increasing the awareness within that disease community and trying

to align their efforts and so they move forward more and there's less of -- kind of I'll call it a kind of inefficiency that they may experience from efforts going on -- different efforts that are not coordinated as well as they could be.

Communication, education and outreach -- here again, building on that expertise that we see most groups have in terms of being able to communicate to their stake -- their own stakeholders, their own constituents as well as to others -- groups can conduct surveys of the community to collect that kind of comprehensive representative input and -- and we anticipate that the guidance we're going to be developing and issuing in June, the draft guidance, will be very helpful in terms of suggesting ways to go about doing that.

But you can do those kinds of surveys of the community to better understand what it's like to live with your disease, the available treatments and accessing and participating in trials and perhaps other issues of concern.

If the group has -- we also think it would be

very helpful to educate communities about the drug development process and the medical product device and biologic development process so people are aware of what kinds of research have to be done.

What kind of questions have to be answered about safety and efficacy and being able to manufacture a drug once you've developed an experimental compound? Can you manufacture it in a consistent way so it delivers with the benefits that were observed in clinical trials?

And what kinds of timeframes are involved with that and then when are opportunities to get involved and -- and help with developing tools and so on to -- to run effective programs -- drug development programs?

We also think the groups can conduct that other kind of outreach and in a number of other venues we've talked about the need for a general cultural change across the whole drug development, you know, ecosystem and probably healthcare delivery as well.

And this is again where our communication of what's going on here in the voice of the patient and drug development. More needs to be done to implicate

this message and understanding in -- in regulators around the world, academic researchers, regulated industry and in healthcare delivery -- so there's a lot of work to do with just trying to continue to reinforce the message and external stakeholders are very good at helping with that.

In terms of convening meetings, certainly the externally led patient focused drug development meetings are one type and they are extremely helpful and we are committing again the guidances we'll be developing will maybe help with other types of work that groups may want to convene.

If you have particular scientific and technical capabilities in your organization or access to them, you may want to convene meetings and go after other scientific and technical issues that are creating uncertainties in drug development and could you benefit from additional discussion among a workshop of experts from different backgrounds and industry academia, government agencies and so on to just further structure what is it that is not understood, needs to be better understood, focusing data collection and so on to

reduce that uncertainty to help advance drug development in that area, or related to that issue.

And finally, contributing to guidance -- I mean patient groups. So the FDA is developing guidance -- I have two flavors -- I'm going to be very simplistic here but there are two flavors of guidance that I think of that we might develop and one is sort of a disease focused guidance.

And the guidance we might develop in a disease area will tend to be intended to address and provide a broad treatment of issues in that disease area. It won't get into lots of specifics within sub-groups. It'll have broader coverage.

And if we have a methodological guidance that we might put out -- maybe statistical methods or pharmacological methods and so on -- then again, it's going to be a general treatment of the methodologic issues and it'll cover a range of study settings, patient populations and so on.

And so there would be a -- a way to enrich those guidances would be to -- and external stakeholders would be perhaps well positioned to -- to

work to develop more specific use cases or scenarios. For example, in the case of a disease guidance where you tailor that guidance or you suggest additional considerations or particular considerations related to an important sub-population who has that disease, maybe it's related to patient age or the severity, you know, stage of disease, the severity of co-morbidities that they may experience or other considerations, that are very important considerations, within a given disease area and are not going to get treated in any depth in a general guidance document.

Similarly, methodological guidance would be able to be enriched by examples of considerations where that method may not be particularly applicable to a certain sub-population or a certain study setting.

Maybe looking at variations in economic or cultural contexts that are relevant to people with that disease, language ability, literacy, numeracy and so on or mobility. So issues related to these kinds of considerations could be further explored by an external group and that could be added to help further, you know, kind of adjust or refine the approach someone

might take and include received information like that. We can try to figure out how to integrate it maybe as an annex to guidance that we developed that's more general.

Here are some examples of questions that we thought up at our -- again external groups are better positioned perhaps -- might be very well positioned to address that would be extremely interesting to us and we'll be probably elaborating on some of these in our -- our session in a few minutes.

The first is the one we've been talking about a lot and it's just so central -- which is, what are the disease impacts that matter most to patients, you know, and how does that vary by socio-demographic factors, you know, by subgroups -- maybe a pediatric population or a geriatric population or other populations that have a major co-morbidity along with that disease of interest, stages of severity or other like circumstances that can affect what's most important.

How does that -- how attitudes toward or tolerance of risks and uncertainties about side effects

may vary by sub-population. Again, same kinds of just repeating similar kinds of sub-populations by culture, severity and other circumstances that are important to understand.

How well do the most commonly studied endpoints in current clinical trials align with the things patients are saying matter the most to them -- the impacts are the things they care about the most and how does that value what might be a better way to go about what studying -- what matters most?

In our currently conducted trials excluding patients who really want to be participating because the enrollment criteria exclude them -- not intentionally but that’s the way it works out, what might be done about that?

Our current trial protocol is intolerable or otherwise not workable for patients with the disease who would like to participate in the trial might otherwise be eligible. How can you measure and increase the likelihood of the patient enrollment and likelihood of patients for staying in trials in a given disease area?

What challenges do patients face when they're trying to adhere to a prescribed regime of treatment and again probing more into how does that vary by patient sub-population and ideas maybe for how to address this?

In addition, post-approval -- how well is the current labeling communicating information that patients need to know in order to use drugs safely and effectively -- and this is another area which we think a lot of valuable contributions could be made and insights that would allow -- it would be information that would inform FDA in terms of future actions and perhaps future policies. So I'll stop there, but this is just to give -- it's certainly not exhaustive but it's meant to give -- be illustrative of the kinds of things we think external groups are especially well positioned to help us with and I'll turn it over to Keith.

MR. FLANAGAN: Thanks Theresa. So this is sort of what is guidance 101 or 001 -- just kind of the very basics -- we're going to talk about what is guidance, a little bit about the -- a little bitty bit

about the substance, the process, some practical considerations and then give you some big picture context.

So a guidance document represents FDA's current thinking on a regulatory issue. The guidance is prepared for FDA staff, industry, external stakeholders and the public. We issue a draft, consider public comment then finalize the guidance.

Guidance may/should be updated as the science in the field progresses. It's not legally binding but shows one way to achieve the regulatory goal. Industry may take an alternative approach that complies with relevant statutes and regulations and FDA staff may depart from guidance documents with the appropriate justification and supervisory concurrence.

So substantively what type of information is most useful and relevant for guidance development? In a nutshell -- information that could bring in the patient's perspective to specific drug development and regulatory challenges -- Theresa's slides 35, 36 and 37 give you a little more detail on that and panelists will dive down into the weeds momentarily.

Procedurally what are the main windows for you to provide input concerning guidance? And the four main windows are as follows: First you can suggest that FDA revise or withdraw existing guidance documents. That's not the focus of today's discussion but it's very important.

Sometimes instead of blazing a path forward we need to refine, update, just fix, correct, our prior work that's hanging out there.

Second, you can comment on a draft guidance that FDA has issued. Third, the topic of today's meeting -- you can submit drafts and proposed guidance documents for us to consider.

And last, you can suggest specific issues on which FDA should undertake guidance development, explain why a guidance document is needed and in that case, it's most helpful if you can provide information that's useful and relevant in the guidance development.

So just a few practical considerations -- first, considering FDA's role and responsibilities, if you send us a draft guidance to consider, we should not and won't rubber stamp it or just act as a mere

conduit;

If we find that the proposed guidance content is ripe then FDA might develop it into a guidance of our own. It will be informed by your input but ultimately FDA needs to make their regulatory decisions.

Second bullet point their concerns novelty and complexity and difficulty. Not every issue is easy, right? So sometimes internally we can agree or all of us can agree on 80% of a given issue but the 20% of it may be very difficult to resolve.

In those cases, we sometimes want to issue a policy about the 20% promptly and work on the remaining 20% that needs to be deferred until the science is better developed, circumstances change and so on. We may potentially do a separate guidance on it later.

Third thing -- we go on regulatory issues and issues related to specific submissions. Sometimes FDA gets jammed up by legal or regulatory issues or issues related to specific submissions that you can’t see on the outside and we can’t talk about.

But the point is delay or omission of a key

sub-issue does not mean that we are ignoring or rejecting your suggestions. It means additional work or information is needed to arrive at a good answer or we have some other interim road block at the moment.

And then finally after you send in a proposed draft guidance for FDA's consideration, naturally you'll be curious concerning its status. So we were at capacity to provide status updates on demand.

And in fact, that takes us away from a focus on the substantive work. We also cannot communicate one policy to one party before another and we have certain procedures we have to follow before communicating official policies to the public.

And finally, just to give you some -- a little bit of big picture context, we are working on a pilot project to develop and issue bulleted guidances rapidly. That means bullet points on critical elements of drug development.

It means focusing on need to know rather than nice to know stuff. We're very strongly committed to expanding our issuance of disease indication specific guidance. For example, the Division of Neurology

Products recently developed five so Ellis and -- that's from Ellis and Naomi's ODE and they may be able to comment on what we found -- what kind of input we found most helpful.

A focus on the critical elements, streamlines or guidance development process makes it faster and your input can be very helpful in that regard.

That's it Sara.

MS. EGGERS: Thank you very much Keith and Theresa. I'm going to moderate this discussion from my chair right here because yes, it is possible to have a bowling injury and I have one. It hurts to stand for a long time so I will be sitting here but I think I can see everyone on the panel and I can see over there and you as well.

The second thing I'll do before I'll start is I'm going to do a favor for my colleagues and I'm going to give the disclaimer on behalf of all of us that the -- that the discussion we have and the perspectives we share are our own and do not necessarily reflect the position of our employer, the U.S. Food and Drug Administration. Let's see how closely I got to the

standard disclaimer on that one -- because this is really complex stuff we're talking about and it's still evolving and things are moving along.

What we want to do first is focus on expanding upon what Theresa presented about how and why patient experience data can complement what we know internally and what we can get from the science and the scientific means about -- that can inform drug development and regulatory decision-making more -- more generally.

So we're looking for examples of areas where patient experience data might be particularly helpful and then some of your insight into why for that. Theresa had a long list of things including patient experience with disease, clinical trial consideration, et cetera.

And so I will, to prompt our discussion, keep it moving. We'll go through some of those areas. I'd like to first start with talking collectively about patient experience with disease and disease burden. Here we might need chief complaint as we're talking about it, you know what is most impactful and burdensome to patients as well as the broader impacts

of the disease and condition.

And so I'm going to ask Laurie to kick it off and see if you can elucidate some types of -- of experience insight that might be particularly helpful for patients and patient stakeholders and why.

MS. MULDOWNEY: Sure I can get started. Well I think one of the important things that needs to be considered is first what is the drug development landscape in that disease of interest and really thinking about the unmet need before you are determining what type of information and ooh, that determines that information is going to be most helpful to us.

And I'm sort of -- I have spent some time in the rare disease space so I'm thinking in the rare disease space where, you know, there are often times when there is nothing available -- there are no available treatments, there's really nothing even in the pipeline so the need is large.

And we have very little understanding and not well documented natural history. So then we're going to just -- we're really talking about what are the most

bothersome signs and symptoms of this disease, what would be important to patients/caregiver input on what they are seeing.

And I'm thinking a sort of specific example I think where a patient input was really helpful -- and you know, with a group of diseases that inborne areas of metabolism that can result in substrate deposition and it can lead to organ enlargement. And you know, we were looking for, you know, what were the symptoms of this you know, how can we sort of, you know, that's a biomarker for measuring that organ and with what's clinically meaningful to patients and we were able to actually get a lot of patient input on a variety of things including how potentially spleen enlargement could result in bloating, generalized abdominal pain, inability to bend over, and inability to button pants -- so certain things like that that really took a lot of context from the patients for us to understand which was really helpful.

I think if in the position that there are treatments available then you have to sort of identify you know, where all those remaining on that need so

there's certain sub-populations that haven't been met by the treatments that are available or they're residual signs or symptoms of the disease that are not addressed through the current treatments as well.

And sometimes this also could be related to adverse events, or other side effects of the treatments that are available potentially really impacting compliance and maybe that's not as -- you know, it's really obvious to the patients and to the patient's family but it may not be blatantly obvious to us.

We're thinking well there's this drug in clinical trials, you know, this is what it showed but then after the fact, you know, maybe we come to learn that patients really aren't staying on the therapy the way that we think they are because of side effects that they're experiencing.

So those types of things -- so again I think it really first is what is that landscape? What are the unmet needs and then, you know, the patients and the caregivers, you know, there's so much rich information that can really only be obtained by those groups so that's really what we're -- what we're

looking for.

MS. EGGERS: Thank you Laurie. We're going to go to Susan a lot -- Susie, because of your rich experience and perspective on pediatric considerations so I'd like you to weigh on this as well.

MS. MCCUNE: Well thank you very much and as you said what you're going to hear from my discussion today is really going to highlight some of the unique issues related to the pediatric patients and their families.

One of the things that we talk about in terms of bothersome signs and symptoms is related to the fact that pediatric patients may actually appreciate symptoms very differently. Something that an adult might not think is important may be critically important and bothersome, especially to an adolescent, especially related to body image or related to invincibility.

In addition, some of the things that may impact their ability to function in school -- go to certain classes or participate with their friends. Also, on the family scenario something that keeps the

entire family up at night in terms of coughing -- that might not be quite as problematic to the patient, maybe terribly problematic to the parents and the other siblings who can't function the next day because they've been up all night.

So those are just some very brief highlights but something to consider in terms of -- of all of these bothersome signs and symptoms that may be very uniquely different in the pediatric population.

MS. EGGERS: Great, thank you. Go ahead Naomi.

MS. LOWY: So I just had a comment on the flipside you were talking about -- the coughing. We actually had our patient focused drug development meeting in this room a year ago for patients with autism. And one of the, I think, most interesting things we learned at that meeting was something that's stimming -- which are these repetitive movements in patients with autism and we're talking about the fact that there are drug developers who are developing drugs to reduce stimming and the patients who were at the meeting said, "No, we don't -- that decreases our

anxiety, please don't develop drugs to reduce stimming," that that's -- they like that behavior.

So what may be a bothersome symptom to others, may not actually be bothersome to the patient themselves so from that perspective it's crucial that we understand what the patient perspective is.

MS. EGGERS: Okay, thank you. Yeah, go ahead Ellis?

MR. UNGER: I mean this question is about the chief complaint and I remember many years ago when I was an investigator in IH, I'd be confronted with patients with various types of cardiovascular disease and they'd come in and they'd say I have these 7 symptoms.

And I always say, "Okay, well tell us if we could only fix one, which one would you like us to fix?" And they would -- they could come up with one. Sometimes there was a tie. Then you could say, "Okay, if we could fix that, what would be the next thing?"

So in other words, they could prioritize the multiple symptoms that they were experiencing and I've -- again my opinion, I've been a proponent of end

points that prioritize based on what an individual patient says when they get enrolled in the trial.

So you -- we say to you these are the 6 symptoms in asthma that patients tend to have or these are the ones in heart failure or whatever they are.

We say we want you to put them in an order because we're going to -- we're going to weight your response based on what you said was important to you. There are scales -- there's one I like to talk about for prostatism -- those are generally elderly men who have trouble passing their urine and there's a scale called -- I love this -- it's the IPSS, International Prostate Symptom Scale or Score.

So it asks you know, I don't know -- 13-14 questions. Well if you look at those questions, some of them would be relevant to a given patient but others are not. And what happens is you get a huge signal -- excuse me, you get a huge amount of noise that can drown out the signal.

Because if the only problem that they have is they have to get up three times at night and it's driving their spouse crazy and their spouse is going to

kill them -- that's what they care about.

So in terms of how the public could help us -- I think the public could help us if they could say, "Look, these are the symptoms." If we were to adopt an approach like this for some diseases -- not all diseases lend themselves to this approach.

But for diseases that do, if you could tell us well these are the symptoms that bug us, okay -- this is what's important to a boy who has Duchenne Muscular Dystrophy.

Then we could construct end points that allow all of those various aspects to be considered.

MS. EGGERS: Okay, thank you, go ahead Laurie.

MS. MULDOWNEY: Yeah, I just want to follow on that for a second and I think this was from another patient focused drug development meeting actually and a disease that you know, had a laundry list of devastating symptoms associated with it.

And you know it was -- you know, no cognitive declines, seizures, and the list went on and on. But family members described the loss of language as being just critical -- that both for the patient and for the

families and that was really important and helpful information.

And now sometimes we're constrained by the mechanism of action of the drug that you're creating and we don't expect that it's going to impact what may be the most bothersome sign and symptom but it's -- but to at least have those things sort of identified and that should be part of that decision-making when you're deciding what the end point hierarchy might be.

MS. EGGERS: Then you have the issue of finding that intricate balance between the science and the realities of the drug development, and what's really important to -- to patients and their families. Okay, let's move on to talk about natural history of disease or condition and how -- what the patient stakeholders and working with patients can do to provide insight that might be particularly useful.

I'm going to ask Larissa to begin that one.

MS. LAPTEVA: Thank you. So the previous discussion about the chief complaint and the clinical manifestations of the disease is probably a nice segue to the topic of the natural history studies because

good understanding and comprehensive knowledge about disease's natural history is really foundational and fundamental to any successful project development program whether it be a drug or biologic or a medical device.

In order to treat any disease effectively one needs to understand its symptoms and its science and the sequence of symptom appearance and the rate of the disease progression, and all the important to patient manifestations and not only that but also molecular mechanisms that underlie those clinical manifestations.

And all of this needs to be learned and observed and this observational knowledge accumulation can be done so conducting natural history studies in which I believe our patients could really play a central role in helping to collect those data about the natural histories of their diseases.

A well-designed natural history study not only designed by investigators but could really be helped by patient input where patients could potentially be treated as equal partners in the trial design.

And in the design of the natural history study

I think really is a golden opportunity to collect credible data prospectively and sometimes retrospectively because those data could be extremely helpful in product development.

Now natural history studies in general could be very informative for many aspects of one's disease -- they could provide a whole range of phenotypic manifestations as well as shed light on various genotypes of the disease they could help to understand and better evaluate variability in the disease presentation not only inter patient variability which is different among patients with the same disease but those that are intra patient variability which is how the disease changes and progresses within the same patient during the course of progression of the condition.

But in addition to that predictive factors, clinically and laboratory we will love the word biomarkers which is a very general term I think, but predictive markers of what is important for the disease and how you could predict different changes in the condition that could be identified through the natural

history studies.

Clinical end points outcome measures that could then potentially be used and product development could also be obtained and identified from the data resulting from the natural history studies.

Well, in addition sometimes it is important to remember that untreated diseases have their own background risks and when we look potentially for a risk tolerance with product development it is important to remember that there are some background risks that may be there that are maybe even more significant than the potential risks from a newly developed therapy, so natural history studies do provide that information.

And from the perspective of product development as was mentioned earlier, natural history studies are important -- and we've seen it time and again in different development programs. They are an important support for recruitment in clinical trials and the recruitment in product development programs.

I think all of these various beneficial features of natural history studies really apply to any disease or any condition in any development program yet

I think they're particularly needy for poorly-defined syndromes -- for categories of patients with rare diseases.

And this is where one could potentially envision really an opportunity for patient communities to help with designing natural history study to help with recognition and really indication of the important manifestations for specific diseases or conditions. How does data need to be collected? How the study visits may need to be scheduled? How, perhaps, certain poor outcomes could be expected or could be prevented with interventions at different stages of the disease.

Patients -- we're always talking about how well patient's position. I think in this case, patients are really best positioned to help with the data collection and design of natural history studies.

So this is something where we could potentially envision the draft guidance development for natural history study design in the various conditions and diseases.

And it's also, I think, important to remember that patient participation in natural history studies

go far beyond just, you know, putting together a guidance and sending it to us.

It's really, you know, having a patient representative of two or more being part of the research team to not only help design natural history studies but also help to conduct them because they are the best to understand the nuances of data collection, to understand the nuances of how symptoms should be monitored.

And at the end even to help with the interpretation of the data that have been collected through natural history studies. So I just want to make one last comment.

Sometimes when in product development it is infeasible or difficult to advance a COA for various reasons to include comparative placebo arms, natural history studies could be used as potential control and compare it to our data and I'm sure you've heard about folks talking about a platform trials where natural history studies could really be one important contributing feeder into those platform developments where a natural history study did a -- particularly for

a small patient populations, could really speed up our product development, thank you.

MS. EGGERS: Thank you Larissa, yes, Susie?

MS. MCCUNE: So thank you, I just wanted to add on to Larissa's comment about variability and just remind folks about genetic polymorphisms and particular sub-types of disease where -- especially in the pediatric population the disease manifestations may be more severe in the pediatric population and the serious or life-threatening manifestations may be different in the pediatric population than they are in the adult population. So I think those are critically important things to consider as you're talking about natural history studies.

MS. EGGERS: Thank you, and this -- those are two lovely reminders to all of us here that -- that patient experience data includes experience and that we have to -- we have to move along the drug development knowing -- trying to know as much as we can about the science as well as as much as we can about what's important about the priorities that are important to people, so thank you for those examples.

Does anyone else have anything about natural history they want to contribute? Okay, clinical end points and meaningful outcomes -- this is one that we expect would have a lot of interest by stakeholders in -- in discussing further.

This is information that could come from patients and external stakeholder groups about -- that could help inform the selection development and use of -- of clinical end points and outcome measures. So Ellis, you started off something that was related -- do you have any more you'd like to say about -- about how patient input could help with end point?

MR. UNGER: Sure, I mean there's sometimes when it's -- when it's pretty obvious what the right end point is. If you're developing a drug to prevent migraine headaches, you count migraine headaches -- that's a pretty good end point.

It's not very controversial but if you're developing a drug for heart failure --

MS. EGGERS: Um-hmm.

MR. UNGER: It's very different and I don't think we've done a very good job collectively. The FDA

and the medical community at developing end points for diseases -- well heart failure's a good example of such a disease where we haven't done such a great job.

So you know, we approve drugs based on numbers of deaths, times of death or time to hospitalization and we can congratulate ourselves because if the drug beats placebo then we feel like well the drug must be effective if it keeps you out of the hospital, it keeps you from dying, that's great.

But if you take two patients -- both of whom will live exactly 10 years and both of whom will be hospitalized in exactly one year -- one could be living a very fine existence and be happy. The other one could be miserable and unhappy and that's a lot of information that we're essentially leaving on the table.

And there needs to be a way to extract that information because that's obviously what's important. And we have a way of measuring a patient's function in heart failure. We say we want you to walk for 6 minutes and we're going to get out a yardstick and see how far you walked and farther is better.

So that's done, but you know, that's not what patients go -- a heart failure patient doesn't get up in the morning and say, "I want to see how far I can walk today in 6 minutes, I've got my fancy watch." That's not what matters to them. What matters to them may be that you know, they can't walk up that flight of stairs to get into their daughter-in-law's condo anymore so they can't go and visit anymore -- that's what matters, right? That's what matters.

So we need ways to extract that information and we're very -- we're very sensitive to the need to do that. So once again, for some diseases -- not all, but for some diseases, we really need to know what's important to patients.

So all of it is fairly obvious -- heart failure -- I mean if you've treated heart failure -- I've treat heart failure, it's pretty obvious what's important. But for diseases that are you know, less common where we don't have medical expertise here, we really don't -- we don't have a clue -- I didn't say that, but we don't have experts in every -- in every aspect of medicine, we can't.

We just can't and the diseases are rare and the doctors are rare so we need -- we need help. And I think that's where all of you can come in.

MS. EGGERS: Alright, thank you -- Elektra, from your -- from your perch in clinical outcome assessment staff.

Ms. Papadopoulos: Thank you, so I think it's first important to understand that the term "patient centricity" is not equivalent to or synonymous with a patient reported outcome. And so the definition I like to share is the patient centered outcomes is one that Dr. Donald Patrick presented in 2013 where he defined patient centered outcome as an outcome that is important to patient's survival functioning or feelings as identified or affirmed by patients themselves or judged to be in patient's best interest by providers and/or caregivers when patients cannot report for themselves.

On the other hand, a patient reported outcome is a measurement based on a report that comes directly from the patient about the patient's health condition without amendment or interpretation of the response by

clinician or anyone else.

And so from this we can see that patient reported outcomes are really just one category of clinical outcome assessments and clinical outcome assessments include several different types which can be used to measure clinical benefit including how patients feel, function or survive.

So, I'll, you know, give an example. Patient centricity -- patient reported outcomes can actually lack patient centricity if they assess things that aren't important to patients. And so this is why it's so critical to obtain the patient input and voice when developing patient reported outcomes.

And conversely outcome assessments that are not patient reported are often the most appropriate depending on the disease, the target population, you know, other types of outcome assessments might be used.

For example, drugs can be approved on the basis of clinician report or caregiver reports or other types when the patients cannot report for themselves such as young children or those with cognitive impairment.

And so -- just touch on a couple of anecdotes. In some areas, for example in the realm of ophthalmology where appearing in some rural public for that -- what's being captured and measured often doesn't really truly reflect the patient experience so the snow and eye chart that we, you know, that we've seen used doesn't really capture the full patient experience and so patients are interested in something called "functional vision" which goes beyond the visual acuity test but reflects how patients really use vision in daily lives to interact with the world.

And so one, as an example, was a gene therapy that was approved for a specific inherited retinol dystrophy and the primary end point captured this concept of functional vision and actually served as the basis for approval and basically consisted of an obstacle course that patients completed in different lighting conditions.

I -- I find that fascinating. So it used a clinical outcome assessment -- performance outcome assessment to really capture that patient centric concept of functional vision.

In other areas that we're seeing a lot of interest are the use of activity monitoring devices and these have been proposed in chronic diseases like chronic obstructive pulmonary disease, you know, patients with chronic arthritis and others to really get a sense of what patients are doing in their daily lives and really to understand their activity -- their mobility for example in their natural environments outside the clinic.

And oftentimes patient reported outcomes are used in conjunction to accompany these, you know, activity monitoring end points to understand, you know, what effort is actually being expended and what symptoms patients might be experiencing as they're going about their activity and so we see these methods used in conjunction with each other.

MS. EGGERS: Okay, thank you. Susan, we want the pediatric perspective on this.

MS. MCCUNE: Thank you very much. This is really important because if you look at the drugs that have been approved and that are studied in the pediatric population -- approximately 40% of the time

those trials fail.

And the question is -- is it truly that the drug does not work in the pediatric population or do we just not have the right end points or potentially the right dose for pediatric patients?

In terms of clinically meaningful end points, they may differ substantially in pediatric patients. So Ellis talked about the 6-minute walk time, but if you have a 5-year-old and you put them on the path and tell them to walk, they're usually walking somewhere behind you and it's a little bit hard to -- to do those tests.

In terms of pulmonary function tests, they just may not be able to follow the instructions and may not be able to do those kinds of tests. In terms of clinical outcome assessments or patient reported outcomes, it's really critically important that patients and parents together develop reported outcomes that are important for pediatric patients.

In terms of as snapshot in time -- a lot of neural developmental outcome measures are coming to the clinic at the age of 18 months or two years for a test

where they have to be tested all day. It doesn't take into account the fact that they've been in the car all morning -- that they have a cold, they haven't had their juice and they really don't want to do the test that you want them to do.

So in terms of pediatric populations, having the capability of having parent or patient or even clinician reported outcomes through the spectrum of their development as opposed to a snapshot in time would be critically important.

And then something that I think we don't really take into account enough is what's important to patients and parents in terms of timing of things. An example that came up was talking to a parent about what amount of time would be important for them to forestall the onset of the disease if they were giving a preventive drug.

And most of the clinicians in the room said, "Oh, six months would be a good amount of time." And the parents said, "I'm sorry, I have a 5-year-old and every week that goes by that they can be developmentally more mature is important for me."

Now the answer might have been different if that had been an adolescent patient and it would not have made such a difference in terms of the developmental milestones.

But clearly, understanding what the impact of that pediatric patient is -- and I'll just make one comment that I hadn't planned on making to Ellis about migraines and this is totally a personal story.

So my son had migraines starting at the age of 7 and while having migraines and treatment and not having migraines is a good end point, the problem with the pediatric trial was that the placebo rate was incredibly high and they couldn't show a difference in terms of the treatment.

Well the end point was really whether you had migraine symptoms at 4 hours. Well my son had classic migraines so he would wake up in the morning, feel horrible, would throw up, then would tell me he was going to go to sleep.

He would sleep for about 20 minutes, wake up, throw up, sleep for 2 hours, wake up and it would be gone.

So I can tell you that he absolutely would have been a placebo responder in that trial. So I think, you know, understanding the population that you know, maybe migraine is a little bit different in the pediatric population than it is in the adult population.

So every time we think about doing pediatric trials, really understanding what those -- what those end points are and how they might be different and how we might be able to capture them more successfully in the clinical trial setting.

MS. EGGERS: Thank you Susie, that's also a reminder that it's not always so much what we should be using as an end point but how much of that end point we need to see -- how much change we need to see in that end point before we say that that's appropriate as an end point or that's meaningful as an end point. I'm going to turn to Larissa for perspective from the biologics.

MS. LAPTEVA: Thank you. I actually would like to expand a little on what Ellis and Elektra said earlier and this is really about using different the

end points in different therapeutic areas.

And what we clinically observed with some of the practices which maybe a feasible approach -- it may not be a bad approach but is an approach that is not uncommon is that for conditions for diseases that are not well described, poorly defined syndromes.

Many of them may have very different etiologies and very different disease courses yet they may have a common end stage disease course and, if a clinical end point or an outcome measure is developed based on the manifestations in that very late disease course or disease stage, then such an outcome measure could potentially be applicable from one patient population to another patient population.

What we see continuously is that people adopt end points from one therapeutic area to another therapeutic area and the situation was this -- is this. These end points may be clinically meaningful and they've saved many days from many drugs, yet what sometimes is lacking is the sensitivity to change in the individual conditions as well as difficulties with discriminatory capacity of what happens was that the

end points in clinical trial in the population in which that end point really didn't come up originally from and which it wasn't developed.

So I think a real opportunity with use of patient experience data for us today and in the upcoming years, is to try to find those end points that are early end points -- the end points that are sensitive to change in specific conditions and that are reflective of true clinical meaningfulness of the new treatments that are specific for the disease.

Because the more sensitive to change and predictive and discriminatory end points we have, the better treatments we will eventually develop.

MS. EGGERS: Thank you Naomi, anyone else on -- on meaningful outcomes? Okay, well we'll move on because we have still quite a few more to cover and then the next one is -- is patients and families' perspectives on acceptable trade-offs of benefits and risks. I think Susan, we'll start with the pediatric perspective.

MS. MCCUNE: Thank you very much. I just wanted to remind everyone upfront as we're going

through this discussion with respect to pediatric patients that additional safeguards for children, which is 21 CFR 50 Part -- sub-Part D must be considered when pediatric patients will be enrolled in a clinical trial unless the risk of an interventional agent are no more than a minor increase over minimal risk.

The admission -- the administration of an investigational -- sorry, agent, in children must offer a prospect of direct clinical benefit to individually enrolled patients. The risk must be justified by the anticipated benefit and the anticipated risk benefit profile must be at least as favorable as that presented by acceptable alternative treatments.

And additionally, adequate provisions must be made to obtain the permission of the parents and the assent of the child. I just wanted everyone to kind of have those as the ground rules from a pediatric perspective.

MS. EGGERS: If that's your area in your sphere, go look at that. Go look further in that regulation statute. Theresa, would you like to comment on this?

MS. MULLIN: Yeah, just to underline -- not on what Susie had to say but just to underline the -- our learnings from the patient focused meetings and other work, CDER (inaudible) you know, work in looking at patient preference, elicitation in some areas as well.

We know that the tolerance or acceptability of risks in exchange for some described benefit can vary a great deal within a patient population with a given disease by you know, where they are, what the stage of -- a stage of progression and perhaps even more so, life circumstances and even prior experience with treatment.

And an example of this that we had early on in our work with patient focus was when non-cell -- non-small cell lung cancer where we asked a question about preferences of -- for treatment, and the patients who were there who were for example there were a few patients who were mothers of children who were probably in their 30’s or 40’s -- they had children who were still pretty young.

And they were feeling it was -- they would undergo just about anything if it would give them a

little more time to be with their family and live longer for their children. So for them and they hadn't maybe undergone as many courses or different types of treatment.

We also had some patients who were maybe in their 60's or 70's or so and they had undergone treatment previously and were at different stage of their life and their willingness to accept very severe at -- you know, very serious side effects to prolong their live -- of the same amount of time was their tolerance for finding that acceptable was much less -- much lower.

And so it was just to illustrate this. So it's important in a given disease area that -- that we understand that and that that kind of background and context is very helpful if you were studying a disease area to really understand in a given area perhaps, which factors are most important to consider.

It might be able to do some -- some studies and survey information to figure out which factors are the most important in a given population of patients affected by a disease to help -- to help guide and

improve the quality of work that's being done in that area.

MS. EGGERS: Thank you Theresa, Larissa -- perspective on biologics?

MS. LAPTEVA: Yes, I would agree with everything that the previous speakers have said and I think that measuring trade-offs and patient preferences for health outcomes is really a very important area and this is the area where we're still largely lacking systematic data collection and therefore systematic knowledge on how and when certain trade-offs would need to be made by patients or by their families.

And we probably all recognize the different diseases would bring different trade-offs for people if someone has a severe life-threatening and readily progressive disease their trade-off for any given treatment could potentially be different from someone who has perhaps a chronic disease of mild severity with waxing and waning course.

Another I think, aspect here to consider is that different stages of product developments, trade-offs are also going to be different for those who

participate in clinical trials and for those who use a product -- a newly approved product to maybe a product with sufficient history in clinical practice.

Because when somebody's starting say a clinical trial which is an early trial with a new product development and it could be any product could be a drug product, could be a gene therapy or could be a cell therapy or a biological device -- their trade-offs will have to be made, potentially on some theoretical knowledge of what will be anticipated in terms of the benefits of that new investigational therapy and the risks that may be known from previous studies and maybe non-clinical studies.

Whereas somebody who has participated, say in a clinical trial, for six months they have experienced the product. Their trade-off of whether to continue this product later may be very different because if they've experienced some toxicity with the drug, they have experienced the amount of benefit that they could get with the product.

And so their understanding and their preference for the health outcome again will be

different. And we still don't have a good methodology to incorporate this in clinical trials and in product development.

The science of these methods is out there and it's been out there for a while and there has been a number of methods that could be applied here yet we still are waiting systematic data collection.

Now yet when somebody comes to the physician and they are offered a new treatment, their trade-off will again be different. It will be based on some theoretical knowledge but on the knowledge that has been accumulated about the product which now already has known safety profile and efficacy expectations.

So at all of these different stages of product's lifecycles, certain trade-offs would need to be made by product users and we -- we don't -- we still on many occasions don't understand what drives people to choose one treatment over another.

Another aspect of this is to look at different product categories. Since I represent CDER here I get to talk about cell and gene therapies. When a drug which is say an immediate release tablet and the whole

product can be taken and it's out of the system in 6 hours, that type of trade-off and potential for trying the product -- for experiencing maybe potential toxicity or maybe certain benefit again is going to be very different from somebody for example, receiving a cell therapy.

Risk tolerance may not necessarily be just or be product specific, it will also be product delivery related because some of these therapies -- gene therapies for example could, could be delivered specifically to certain tissues and that delivery could potentially be much more traumatic than just taking an oral pill.

So, so these are the types of trade-offs where there are opportunities for us to understand better from patient experience data. And if some of these information and data could be sent to us -- not necessarily maybe in the form of a guidance but perhaps as summaries of questionnaires, or patient interviews or some -- as some other form. It could be quite informative for us to understand the trade-offs in these different settings and incorporate them in

product development.

MS. EGGERS: Thank you Larissa. I'll put the plug in for the methodological guidances that we are developing that will touch upon those technical methodological issues to, to gather that data. But this shows how intricate -- how related all of these guidances are.

Larissa brought up considerations on clinical trials and that's another area that we think is -- is potentially of great interest to patient stakeholders and how they can contribute unique insight into clinical trial development so I'd like to talk about that for a few minutes.

Naomi, do you have any perspectives you can share about how input from patients on various aspects of clinical trials could be helpful?

MS. LOWY: So I think that this is really a unique area for patient input and one I think that we would really all welcome. I don't know -- we do spend a lot of time thinking about end points, chief complaints, things like that but as far as how a trial really should be conducted, I think there is a lot of

space there for help from all of you.

So when planning a new clinical trial protocol, it may be helpful to look back in the question that you had up there before that are there clinical trials in a specific disease area that have been excluding patients who do want to be enrolled? And I think that's a really important question to answer.

There may be historical reasons for including certain patients but maybe the rationale really just is not there. So I think that is worth revisiting. A related question is -- are there clinical trial protocols that are just not workable for some patients who otherwise would be eligible to participate and what could we do in those instances.

And what comes to mind is a study that was published just last week in the New England Journal of Medicine called the so-called "Black Barber Shop City." I don't know if any of you have heard it but I see a lot of shaking heads, but for those of you who haven't heard of it -- it -- the premise of that study is that black men have very high rates of blood pressure and

that barber shops are really uniquely popular setting for African American men to go to.

So they set up this trial to treat hypertension in black barber shops in California, in L.A. and they brought a pharmacist into -- into the barber shops and that serves -- that was where the clinical trial was really conducted.

There were two groups of men, they were randomized to either a group who they were given information on hypertension and maybe encouraged to go see their physician and another group who received that plus they were actually treated with anti-hypertensives and the results were really remarkable.

Both groups had decreases in their blood pressure. The group clearly that was treated with the anti-hypertensives dropped their blood pressure by about 27 millimeters of mercury.

So I think -- I think that provides a really unique perspective in how we can best accommodate patients where patients are comfortable, where we can find patients and also taking the results of that trial and eventually adapting it to the real world if --

because we got such great results in that setting.

MS. EGGERS: Great, thank you Naomi.

MS. LOWY: Sure.

MS. EGGERS: Laurie?

MS. MULDOWNEY: Sure, so to sort of follow on what Naomi was saying you know, there's really the two buckets when we're talking about who's actually participating in the trial or two reasons why patients may not be participating.

And the first related to eligibility criteria and I'll go back to sort of the rare disease space -- for the most part the eligibility criteria that are excluding patients in this space as if -- is often related to the inability to sort of perform -- performance measure that might be that clinical outcome that primary end point.

So I think where there can be input that's valuable there as in helping us again -- it gets back to end points, at identifying things. And Susie touched on this a lot -- 6-minute walk tests, and pulmonary function tests, and tests that are frequently done but can't be done in that youngest age cohort.

And they're really, really challenging to identify, you know, what can we measure. And parent caregiver input can really be so -- so helpful in that instance to try to identify other ways to measure efficacy in those patient populations.

And then that second bucket is the enrollment -- the eligibility criteria. It may be quite broad, but it's -- but people aren't enrolling and sort of identifying why. And you know, the -- a couple of things I would say about that. You know one that I think -- at least in my experience you know, often the clinical trial designs are becoming more complex and oftentimes in these really complicated multi-system diseases, we're measuring a lot of things and we don't always think about the burden that that has on patients and caregivers.

And that can be really helpful information for us to understand if it can offer for the drug company for that matter to help narrow that focus to make -- to try to make trials, you know, less burdensome but still to be able to get the important information that we need.

And then not so much necessarily enrollment purposes, but Susie said something that reminded me of a situation where you know, patients were coming from, you know, all over the country to one or two centers where they would stay for a day or two and get a litany of tests -- many, many, many, neuro cognitive assessments, any one of which might take three hours to conduct.

And what we learned are you know, things that we can learn from patients and caregivers is well my son or daughter is always going to do better in the morning. You know they know their kids, they know what their disease variability is from day-to-day.

And so then you're really talking about the quality of that data that you're getting and if you're blind to you know, if you're not paying attention to that you're not getting that input then that can be really, you know, detrimental obviously to the quality of the data that you're getting.

MS. EGGERS: Thank you Laurie. We could cover these issues in a lot of depth but we do want to keep moving on to talk another question about how -- what

formats are useful for people to submit this data? So I'm going to go to the last one which is communicating labeling information to patients.

So how FDA or sponsors -- how we communicate information and I'm wondering if Ellis or Elektra has any insights on -- to share on that and how patient input or input from external stakeholders could be useful?

MR. UNGER: Well we try very hard to do a good job but it's hard, it's very hard to make labeling understandable to patients. Labeling is really for practitioners -- I'll say that, but it's the practitioner who has to understand the label well enough to be able to then transmit the information to patients -- so it's a critical part of, you know, drug approval and the drug.

And it's hard. I mean sometimes the -- I just try to throw out many examples quickly. Sometimes the end point can be very understandable but the numbers aren't very clear. So if the end point is mortality -- disease has a 20% mortality rate and the drug reduces mortality by 20% wow -- does that mean the mortality

rate goes from 20% to zero? No. It means it goes down by 20% of 20%, 20% of 20% is 4% so there's really a 4% reduction. So that's one way labeling can be unclear.

Another way is these end points that we have some of them are not understood very well by many people. So for major depression we use an end point called the MADRS -- it's a 17-question scale.

And if I said to a psychiatrist that the drug makes the MADRS go down by 3 points relative to placebo -- do they actually know what that means? Can they -- can they talk to a patient in their office and say, "Look, the MADRS went down by 3 points on average." It's very difficult to translate into that -- translate that into something that the patient can understand.

And we have to do better. We, we have to do better. The guidance is really not focused on labeling. Am I correct? The guidance is more about end -- end points?

MS. EGGERS: The guidance that we're talking about today is how patients can provide input on relevant topics to drug development.

MR. UNGER: Okay, okay fine so labeling would

be included. So it would help -- and I'm thinking outside the box here a little bit. But it would help if we had input from patients on what, you know, what -- not so much the label because the label is not for them, but what information would they like to have from their practitioner, okay, about what this drug -- what they can expect from the drug, okay?

So that would be interesting and it's something I don't think many of us have thought about very much but there you go, food for thought.

MS. EGGERS: Thank you, anything to add Elektra?

MS. PAPADOPOULOS: Well I, I really echo what Ellis has said and I think the first step really to a patient from my communication is going back and measuring what matters to patients. For example, a patient reported outcomes that are developed with patient input would be more likely to use patient for labeling which that resonates with the patients.

And so it's important to step back and ensure that the instruments are developed at the outset -- at the outset with an eye toward eventual labeling so that

they will be understood by -- not only by the patients, but of course by the prescribers.

And I think you know, as Ellis said we really need to be open to ways of making information and the labeling more useful to prescribers so that they can then better communicate with the patients and research has shown that you know, patients who are engaged in their healthcare actually have better outcomes so it's extremely important.

And as part of the clear communication I think it's important to communicate the concept that was measured. What was the theme that was measured because all too often we'll see the names of instruments put into the label and nobody knows what was being measured so it's fine to put the instrument name in but also putting that concept in there and communicating what the possible range in score is and what constitutes a meaningful change within that score -- within the meaningful change threshold within that score.

I want to say that there's also you know, patient information that's approved by the FDA that helps patients use the drug product safely and

effectively and FDA's also committed to further new development of patient information and is proposing a rule to require a new form of patient labeling -- the patient medication information for human prescription drug products.

And so this proposed rule would include requirements for a patient medication information development, FDA approval and distribution and the information would be a clear and concise written prescription drug product information presented in a consistent and easily understood format to help patients use their prescription drugs more safely and effectively. So I just wanted to highlight that as well.

MS. EGGERS: Thank you.

MS. PAPADOPOULOS: Okay.

MS. EGGERS: So that was a wealth of information from our colleagues about what is important and why. And we want to close this session by getting some perspectives on what is the best and most practical way for you to share this type of information with FDA and others.

You'll recall Theresa had a couple slides up and discussed the range of ways that stakeholders can help. Guidance was one of them but there was a number of other ways and so the -- the question is, is what's most appropriate for one vehicular channel and when is it more appropriate and more effective and efficient to go another way?

So let's start by asking from the panelists what type of information -- the stuff we were talking about this afternoon so far, might be most suitable to submit in the format of a proposed draft guidance? And so I'll see if, if Ellis or Theresa want to start that off -- Theresa go ahead.

MS. MULLIN: So I think, I think it's hard to you know, kind of answer that question in absolute terms Sara. So, but per what I was saying earlier when I was presenting kind of an overview I think that it could be that for example, for one of these perhaps, bulleted guidances that Keith described, or disease guidance where it alludes -- or it mentions enrollment criteria or it mentions inclusion/exclusion criteria.

There are opportunities I think there to -- to

elaborate on that to do a sort of more deeper set of considerations related to that. That might be an area that could be developed by external stakeholder groups to provide more of that breakout by sub-populations.

We have been talking about you know, various ways to look at stage of progression of a disease, pediatric patient considerations, maybe geriatric patient considerations, other sub-groups that are very important and they have particular issues that affect their -- whether the enrollment criteria that are standard, even work for them -- I was a meeting that Annie Kennedy and PPND had recently and there was a discussion about how few trials there were for boys with DMD once they reached the sort of teen years.

And because they could no longer complete the 6-minute walk -- I'm sorry to keep -- we keep bashing the 6-minute walk, but that's a standard measure that's used.

And that was not something they were generally able to do anymore. So there are things where you could say what else is going on there, what other criteria, maybe thinking of other approaches there that

would speak right to the enrollment criteria that might be used for the inclusion/exclusion criteria that might be used for a sub-population of maybe by age or whatever, for a disease population -- so that's the example I'd give.

MS. EGGERS: Thank you. Would anyone else like to join in on this, we have Larissa?

MS. LAPTEVA: Yes, so as I indicated earlier I think natural history study designs could potentially be sent to us in the form of a draft guidance and also various methodologies on how to measure and collect patient preferences and that would include say methodologies that could be collected for chronic states versus for acute states because the trade-offs there will be different.

I would fully support the different patient sub-populations, pediatric, geriatric -- there will be a challenge that will be presented particularly by folks who actually have difficulties communicating -- those who may be deaf or blind.

You would still want to somehow get the patient preference from those populations too. But

also, one of the reasons why patient experienced data making such a -- what I would call delayed entry into product development is because these methods are typically very complex.

They are complexly difficult to measure. They are very time consuming to incorporate in clinical trial design. And so developing IT instruments -- this is something that is probably universal would be you know, one other potential aspect to which I think we all could benefit.

And the overall draft guidance as we approach it here multi-disciplinary and I'm sure that any draft guidance that's sent to us, no matter what is the topic, would probably need to be development by just one patient advocacy organization but really, a -- a team of experts, and -- and multi-disciplinary contributors.

MS. EGGERS: Okay, so thank you, Theresa?

MS. MULLIN: So I just would like to add -- and just to show that FDA is not a monolith I -- I would think that I'm not sure I completely agree with what Larissa just said.

I mean I think guidance might be an appropriate way to submit that information but it certainly wouldn't be the only way you could submit a natural history study or the kind -- all the information described.

Maybe there's a form of that or a maturity of that that would make it potentially you know, kind of suitable for the guidance, but I think that there's a wider swath of it that I could imagine could be submitted just as research papers or other papers that inform you know, policy development.

MS. LAPTEVA: I completely agree. I completely agree this could be developed. All of these different types of information could be submitted as guidances or as part of data collection summaries -- other potential formats, I absolutely agree.

MS. PAPADOPOULOS: I would also add I think it's really important when the patient experience data is being submitted to indicate how you think this information can be used in medical product development.

And so, not to just sort of give the data to us but let us know what you think it should be used for

and it doesn't -- as has been mentioned does not always need to be in the form of guidance, it can come in different forms.

MS. EGGERS: So let's build on that and what are the other types of areas? How can stakeholders leverage those other areas beyond submission of proposed draft guidance to really help inform -- to add as much or greater value to -- to this area? Elektra did you have other thoughts on that?

MS. PAPADOPOULOS: Well I -- I just wanted to also highlight the need for a methodologic bigger way conducting scientific research and the need to have broad input from you know, scientific experts, methodologists, disease experts, clinical experts, measurement experts, drug developers, you know there's a whole slew as well as the patients and the caregivers.

I would much rather have a group, you know, who has say limited funding maybe write off a smaller project than try to boil the ocean, but really produce high-quality, rigorous research which then you know, maybe others could build upon.

MS. EGGERS: Thank you, others -- Naomi?

MS. LOWY: So, I think that there is an ideal time and place for a guidance to be written but I would say that our -- at least in my experience, some of our biggest “aha” moments have been in direct interactions with patients and meetings with them and advocacy groups.

Having patients in the room directly tell us some of these experiences, I think, has been more impactful than maybe receiving a 30-page guidance. And again, that’s not to minimize the guidance but I think that it is important to sort of figure out what kind of impact we’re trying to make and what -- what you’re trying to convey.

So, those sorts of interactions have been very helpful. In our patient groups whom we have an established relationship with, they’ve, you know, they’ve gone to national or international meeting -- after the meeting they’ll send us their slides or their poster-presentation from that sort of to keep us updated with what’s going on.

I think that has been very effective and

certainly, you know, reports, white papers, those sorts of things. So there is a huge spectrum of options beyond.

MS. EGGERS: For our final minute we have -- oh Laurie and then Susie to close out with the pediatrics.

MS. MULDOWNEY: So I was just going to mention that you know to keep in mind that one of our -- the primary audiences for our guidance is industry. So if you are doing these studies and have this information and you know, I think Pujita gave some examples of how this, you know, this resource -- this information sharing resource will ultimately be used some day, but that's an excellent way to get that information out to industry, you know, maybe in conjunction with a guidance.

You know, there's many ways that that could be done.

MS. EGGERS: Thank you, Susie?

MS. MCCUNE: Well I was just going to pull it together in terms of how all of those groups might come together in a consortia so as an example the

International Neonatal Consortium is a group of stakeholders from patient parent advocacy groups from academia, from industry and from regulators around the world -- over 100 individual institutions coming together to have these conversations within the context of protocols and end point definitions, so.

MS. EGGERS: Alright, well I want to thank the panelists for being up here for an hour and a half and providing really fantastic information. I love being moderator because I learn a lot from you. It helps me in our work and I'm going to see what's helping you. We will take a break now for 15 minutes and then we will all hear from the stakeholder perspective, so come back at 3:15 please.

(Break)

MS. CHALASANI: Good afternoon everyone, my name is Meg Chalasani and I work in CDER's Office of Strategic Programs. I will serve as the Moderator for our second session today which will really focus on seeking input from our patient and other external stakeholders on how best to communicate FDA's current thinking on submitting proposed draft guidance relating

to patient experience data.

We had a really rich panel discussion earlier and we're really hoping to build on that. I just want us to take it a little bit more towards that proposed draft guidance relating to patient experience data scope.

So just a quick overview of the former -- we'll have a moderated panel discussion on what questions would be really helpful for FDA to address in its forthcoming guidance on guidance or guidance styles through submission -- just how we call it internally, followed by a facilitated audience discussion where we'll really seek broader input from all of you in the audience on the topics that we've been discussing today.

So first I turn to our panelists to the right of me and ask each of you to introduce yourselves.

MR. ALLEN: Hi, I'm Jeff Allen, President and CEO, Friends of Cancer Research.

MR. BOUTIN: Marc Boutin, CEO of the National Health Council which is a patient-led organization with all stakeholders in health ecosystem represented

included the biopharmaceutical, generic, diagnostic, family care-giving provider and insurance represented.

MS. KENNEDY: Good afternoon, I'm Annie Kenney. I'm Senior Vice President of Legislation and Public Policy for a Parent Project Muscular Dystrophy or PPMD.

MS. MCCLEARY: Hi, I'm Kim McCleary, I'm Director of FasterCures. We're a D.C. based center of the Milken Institute and we work across diseases with all the stakeholders in the ecosystem to identify and breakdown barriers that add time and expense to the process of getting promising therapies from the bench to patients.

MR. MELMEYER: Hi everybody I'm Paul Melmeyer. I'm the Director of Federal Policy at the National Organization for Rare Disorders. We're a patient advocacy organization that represents all 30,000 million Americans with a rare disease.

MS. PARISER: Good afternoon, I'm Anne Pariser. I'm the Director of the Office of Rare Diseases Research at NIH's National Center for Advancing Translational Sciences or NCATS.

MS. PATRICK-LAKE: Hi, I'm Bray Patrick-Lake. I'm the Director of Stakeholder Engagement at the Duke Clinical Research Institute where I lead the Research Together Program which brings patient and community members together with other stakeholders in the design and conduct of research.

MS. STROBEL: Hi, I'm Mary Jo Strobel. I'm the Executive Director of the American Partnership for Eosinophilic Disorders. We're a 501c3 patient advocacy organization that serves patients with the eosinophilic associated diseases.

MS. CHALASANI: Great, thank you all. First, I want to provide you all with an opportunity to really reflect on what we heard during our Session I, really on the what types of patient experience data would be really useful and in the practical ways to probably share those with FDA and I'll really just ask you to reflect on some of the topics that we've heard so far.

Perhaps we'll start on that end of the table this time, Mary Jo?

MS. STROBEL: I thought it was -- it was really helpful to be here in person and hearing the

perspective from the FDA. It's much different, we were having conversation during break but when you receive that information verbally versus reading something on a document it's -- it's much different.

So my key takeaways from the first panel was it was really helpful to hear about the various stages when that patient experience data is helpful and why. I think patient groups are well-positioned to facilitate that and bridge that gap but may not know or understand when that guidance is the best approach to take or how to know maybe what already would be in the works or has already been submitted to be able to build upon.

Also, considering ways in which to collect data outside of survey or formally design data capture method. Some of the most insightful information may come out of open-ended questions and discussion opening up an avenue to collect that open-ended perspective.

Not just multiple-choice questions on the survey for example, but really to facilitate that open discussion really I think brings the most insightful information forward.

MS. CHALASANI: Thank you, Bray?

MS. PATRICK-LAKE: I thought it was particularly useful to go through the resources and then also kind of see the stage gating of the guidance and development as Mary Jo said kind of mapped to the different phases of medical product development cycle.

But I really wanted to pick up on something I think Elektra touched upon which is that everything doesn't have to be a proposed draft guidance -- that is pretty high buyer for a lot of patient groups and I think the more we can do to help people understand the types of patient experience data, clinical trials, transformation initiative which is an FDA public-private partnership is working on a framework to help assess high-value, high-impact, opportunities mapped with investment which could be time, resources, staff member collaborators -- anything FDA could do something taking that into consideration and moving that forward or proposing its own road map to really help, I think, the patient groups navigate what you can do -- what you can do well, and who you should be doing it with would be particularly useful.

MS. CHALASANI: Great, thank you, Anne?

MS. PARISER: I, I'm coming at this I guess -- a little bit difference perspective than everybody else on the panel. I'm not representing a patient group but rather a sister agency for FDA and we also spend a lot of time thinking about patient experienced data collections.

We heard natural history studies and registry a number of times, so I guess I'm just throwing in a plug here as we're also here to help and we have a number of resources that we built over the years to help you either get started or to further your data collections and we do actually work closely with FDA on a number of these.

But I'll just name a few. We have something called the NCATS tool kit for patient focused therapy development. That's a long name but if you Google either NCATS tool kit or NAH patient tool kit, it will take you to that and this is a collection of tools, advice, documents that have actually been put together mainly by patient groups -- experienced patient groups over the years who have learned through their

experience and trial/error how to put some of these data collections together.

And I'd urge everybody to please take a look at that. You know you don't have to reinvent the wheel. There's a lot of people that have been out there who have done that and I just urge everybody to seek out what exists already before you start your data collections.

Data are good -- particularly for poorly understood conditions such as rare diseases but good data is even better so there's a lot of things that have been looked at or exist. I would just urge you to look at those and if you need any help finding that you could contact me or Google this or contact our office and we'd be happy to help.

MR. MELMEYER: well we at NORD are incredibly pleased with the number of opportunities our patients and patient organizations now have to participate within FDA initiatives and I think that was quite well highlighted by the wealth of opportunities discussed in the first panel just before this one.

It does create the unique problem however in

that many patient organizations could be rather overwhelmed with all the opportunities that are in front of them and are not perhaps sure of which to take and that kind of builds off of Mary Jo and Bray's points and that could be most exacerbated within our community because of the 270 organizations that are rated as these patient organizations that focus on any one single disease that are members of the National Organization for Rare Disorders, the vast majority of them have fewer than five full-time employees and many actually don't have any full-time employees.

They have a volunteer Board of parents and grandparents who are there working for their loved ones. So thinking about how we can structure not only the guidance we'll be talking about shortly, but all of these opportunities to make sure that they're accessible and are a benefit to kind of the full breadth of organizations and their capabilities is something that we're here to ensure.

MS. MCCLEARY: So first, I just have to say wow. Annie and Marc and I were commenting after the first panel concluded that it feels a little bit like

déjà vu but we've switched seats. Like we can remember when we were up here saying these were all the rules that patient experience could be useful and FDA was listening intently, and obviously has taken it onboard into the next level.

So it's very rewarding just to hear all of the embrace.

MR. BOUTIN: Let's give FDA a big round.

MS. MCCLEARY: And I -- I also just want to send up a huge thank you to Theresa's team and the whole team and the Office of Strategic Programs because I think maybe, you know, we talk about the outcomes of the PFDD and the series of 24 meetings and now all the externally-led meetings that are occurring and you know, what we've learned.

But I think one of maybe the unseen outcomes and takeaways from that effort and that initiative has been the ability for FDA to gain both a vocabulary and a venue to understand the patient experience from the patient point of view in a setting that is outside a single product discussion that is not really stressed by that kind of immediate, sort of, you know, literally

life or death decision.

And it has freed up a conversation about all of these different things from outcome measures to what does meaningful change sound like to what should we be putting on the labels so that those prescribers and patients will understand what we mean by, you know, a couple of points on the MADRS score.

So I feel like it's been a huge evolution and now what we have the ability to do is kind of refine from what the earlier colleagues on this panel have said, the ways in which to kind of tailor and match what the needs in a particular disease state are with what the tools that FDA might be able to use and how to -- how to put those things together so that you can package up your patient experience in a way that would really help to advance both the drug development pipeline itself and also inform the decision-making at the agencies level that will take place all along the way.

I do have some specific comments but maybe I'll just hold those.

MS. KENNEDY: So I agree with everything

that's been said previously but one of the things I'd like to reflect on as I was listening to the previous panel and then preparing for this panel yesterday was -- I went back to Section 3001 and was looking at the definitions in that section which I think are really important to set the tone for what we're doing here.

And you know, if we look back a decade ago in our community -- or not even that long ago, maybe even 5-6 years ago, I think when we engaged with industry and we engaged with other stakeholders who sometimes felt like if you weren't at the table you were on the menu right?

But we really had as patients and patient op's groups, you really had to make sure that you had a space at the table so that you were a part of the discussion. And so as we all engaged stakeholders in the 21st Century Care's discussions that was very much a part of the discussion -- how did we make sure that we were broadening the definitions in the framework around drug development and the drug development lifecycle to ensure that we all were being recognized as innovators and those that are now generating data

and sometimes were the ones that probably had the more relevant data sometimes, that needed to be considered.

So you see that now in the definitions. But those definitions and those discussions were never intended to shift the responsibility away from academics and researches and industry just to patients and caregivers and patient advocacy groups -- but to ensure that we all had a space together at that table.

And so I think that's really important for this discussion today that we make sure that we're not shifting the responsibility to patient advocacy groups and patients and caregivers and saying, okay, well any guidance or any of that patient experience data that you're going to do that and fund that with your rock and your bake sale and we'll do this piece.

Because within our community we've had very successful collaborations with our industry partners in figuring out how we're going to move that forward and I think that's really important that we recognize that.

And then the other things is, you know, I was really appreciative of that first panel and especially Theresa's opening presentation where she really started

to lay the framework of what kinds of information are really important and to really set some context.

And as a community we've done a lot of that. We've done much of that and we talked a little bit about, you know, we're going to talk today about development of guidance to help inform how to bring patient experience data in.

That panel talked a lot about the really important impression that the PFDD meetings have made on the individual panelists and their experiences, but I think we also need to talk about many times it was -- just so submit that to us, send that to us, publish that, send that to us -- what does that mean?

So if you're not outside of guidance and a PFDD meeting how do you get published data to the FDA? What is that pathway? What does that look like -- because I think some -- we need to maybe be considering how time sensitive some of that information is and what is the pathway for that and can that be done by a patient advocacy group?

Can that be done by individual academics? Can that just be done by industry? Does it have to come in

with a product submission? And so those are some of the things I think we should be thinking about, may not all get answered today, but things that questions are coming out.

MS. CHALASANI: Thank you Annie, Marc?

MR. BOUTIN: So I want to join Kim and say again, wow! So much work has been done in the last 5 years and for many of the patient advocates in the room, some of us have been at this for 25 years. And to see the speed and the acceleration change just in the last 5 to 7 years is phenomenal, so kudos to the FDA and to the work of the patient advocates in the room to really make this happen.

I want to share two points that I think are important -- one direct to, to the conversation we just had and you've heard a number of people allude to this. We need a roadmap.

When the patient community supported the concept of this guidance on guidance, it wasn't so much that we all necessarily wanted to go out and develop a guidance for our disease area -- it was really we wanted to have a meaningful roadmap on how to get

information out to the regulator and to the folks that are going to be developing products.

And you expressed a number of different ways in which that can be done. I think we have to think about a framework that manages expectations. It creates a hierarchy of what the need is so that any individual organization can do two things.

They can assess where their disease is and really identify where can they use the minimal resources, which includes staff, volunteer and money, and actually have the greatest impact and move the development of new interventions for their condition.

They also need to be able to assess their own capacities. You know, what do they have and what can they bring to the table? As much of that as you can put into the guidance will cause every organization to take a step back and really work through that analysis.

Because what we don’t want is everybody rushing to submit a guidance that is not going to move the field forward. And I think if you can call that out in the guidance, go as far as you can. Many of our organizations will work to develop tools to combine the

existing tools that already are out there to really drive this point home so that we get the most meaningful information out there that we absolutely can.

Second point I'll say -- and how many people in the audience are from industry? Okay, so we have a good group of you from industry. I love you all to death but I'm going to say to the FDA set the bar really, really high.

Now this is a general comment but it's really important. There are a lot of folks in industry that are very taken on the concept of patient engagement, patient centricity -- it's working through a lot of your departments.

But when I meet with your heads of R&D some of them really get it, a lot of them scratch their head and say, "We do clinical trials. We engage patients."

Not quite what we mean. It's critical that this gets embedded throughout the entire lifecycle of drug development. And I hear folks from the FDA say this repeatedly, but we need to drive that point home so that we can push that into the culture of R&D, which

has a lot of challenges in terms of how they think about this.

They're siloed for a specific reason or we want great output. But we in the patient community want to have the opportunity to work with them in the beginning to shape their thinking so that they have right insights and are shooting at the right targets.

Any opportunity you have -- and you've got 5 guidances coming out over the next few years. To drive that point home would be terrific. I remember being in an audience here at the FDA not too long ago when somebody said, "Well, you know what? FDA is not Moses, you're not coming down the mountain with tablets." On this point be Moses, come down the hill with the tablets and if we need to -- we're doing to hit those people within the R&D department upside the head to drive this point home -- it's critical, thank you.

MS. CHALASANI: Thank you Mike, and finally Jeff?

MR. ALLEN: I -- yes, I thought that the discussions during the first panel were, were terrific. They group covered the gamut -- so to speak, of

opportunities and I think it was great to see how many different perspectives from across the agency were -- were represented, so that's greatly appreciated.

I think that the opportunity here was really -- and even the intention of this legislation of including it either it be in 21st Century Care's or in the user fees, was to try and facilitate next steps to operationalize the patient focused drug development programs that started with the 20 meetings.

And I think even the fact that that opportunity is presenting itself shows that the -- the patient focused drug development meetings were able to be conducted in a meaningful way so that it could be operationalized now and not just be baseline meetings to learn more about how different conditions afflict the different populations.

But to now and try and bring the entire field forward in many of those areas -- so the concept around guidance. I hope that we can use that as sort of a -- I don't know air quotes or a little bit loosely to some degree because, you know, I think what -- as was implied that the guidance may be a very high bar or

even an ultimate end game for what to do with some of the information that was described earlier.

And hopefully though, by having that be the focus as a potential vehicle -- that it's not the potential vehicle, that there's other ways to contribute to these processes.

And also, to add -- you know I think like Marc said, this isn't just about the FDA but I think that the desire that the community had in sort of positioning this around guidance documents was -- was helping the FDA be able to articulate different methodological standards that could then be applied.

You know I don't think it's a surprise, particularly, for all the folks that raised their hand from industry that if the FDA speaks first, often they will listen and be more comfortable to move in that type of direction rather than just investing and trying it first.

And some of that's true from our community too. I think being able to understand the information that would be useful, the methodological standards that should be applied allows us to apply our resources and

be able to work within our communities to make sure that we're developing the information that can be most utilized and finally to lay the path forward.

And I think that one of the things that did strike me that I hope that we can add to the discussion here is -- aside from just a process on how to submit this information once it's developed, some sort of process very early on that would allow -- hopefully even informal interactions with the different divisions that we should be working with at the FDA to make sure that we're joining developing key priorities here.

I don't think you -- the agency and the experts at the agency want to receive information that they're not interested in, nor do we want to produce it if it's not going to be useful.

So I think having some ability to prioritize, even for the FDA to be able to ask questions. You know I think we heard that from many of the experts in the first session that there were things that were clearly on the front of their mind that having more information on those topic areas would be really helpful.

So maybe even much like the major medical

center's layout -- the guidance documents that they intend to pursue each year, even giving some sort of idea in terms of burning questions that would be helpful if more data were able to be supplied.

It could help many of our organizations focus our efforts, inform the coalitions that would be needed in order to create that information to bring it back to the FDA ultimately.

MS. CHALASANI: Thank you Jeff, thank you all. I think what I'm hearing is that we're on the right track but there's still a lot of work to do, particularly in helping to communicate more on what's suitable and appropriate and especially practical at what time for a lot of this information, great, thank you all.

I do want to move a little bit more towards the proposed draft guidance -- the guidance on guidance, sorry, the forthcoming guidance. And so when we had calls with our panelists, we asked them as FDA is developing this guidance -- this forthcoming guidance, and if it was to be formatted in a question and answer format, what questions should FDA consider

addressing.

And we heard several common themes and I think they started coming up already. The first one being what types of information on patient experience might be most suitable to submit in the format of proposed draft guidance?

We heard this towards the tail-end of Session I as well as during our introductory remarks right now. And kind of along that line, if external stakeholders do not plan to develop a proposed draft guidance -- whether it's for resources, the time considerations, what are other ways to submit patient experience data related information, including those types of information identified above?

So really what is that range of formats and methods? What is the process for planning and developing a proposed draft guidance relating to patient experience data to FDA? And is there a recommended format or a list of topics for guidance documents that an external stakeholder might develop and submit?

Third, what is the process for submitting a

proposed draft guidance to FDA? There is actually a clear statute for this. What will happen after external stakeholders submit a proposed draft guidance relating to patient experience data to FDA?

So this gets at some of the managing expectations that we heard about, early communication to see if, you know, it's something that FDA even needs getting at those kind of aspects.

And then the final question is something that both Keith and Theresa mentioned earlier is how may an external stakeholder submit proposed revisions to an existing FDA guidance? You don't have -- you may not have to start from scratch from it.

So I think these questions are on the right track and based on the calls that I had with all of you earlier, you agreed. So I do want to ask a few follow-up questions and seek a little bit more -- a little bit more input from folks.

I think we talked about one a lot. In the interest of time I will go directly to the sub-question for two. So is there a recommended format or a list of topics for guidance documents that an external

stakeholder might develop and submit?

I think -- I would be interested in hearing from panelists. How do we really find that right balance of, you know, being -- providing guidance but maintaining flexibility. So would a template be helpful? Or would that be too restrictive or too prescriptive? What are some of your thoughts on that? I think I see Bray -- yeah.

MS. PATRICK-LAKE: Yeah, I mean I think you do need that level of detail and the external resources webpage, I think is -- that's a great start. I mean I looked around in there and -- excuse me, there were -- I mean you can go back and you can look at the Voice of the Patient as a model, but then really getting into developing a meeting plan.

And I think also I'm envisioning some kind of pyramid that shows, you know, what's the highest standard, most rigorous as we start getting -- I mean we have to have the methods where it would come out to, but, you know, the where to start as the patient group and then what you need to work through to get to this level.

I think you're going to have to put it on there even if it's just case examples because, you know, again the capabilities of different groups and the financial resources is key.

And then I also really want us to hit on that. There were statements about -- think about the other stakeholders in the space and we encourage collaborations, but you're really going to have to put that in bold I think with exclamation points if that's really, you know, the consortium model is what we're trying to achieve.

MS. CHALASANI: Sure, so really a question that's going to get the who as well as -- I think the examples you hit right on that I think would be really helpful as well. Others that would like to chime in? I see Anne or Kim and then Anne.

MS. MCCLEARY: So I think that "who" question came up in our protocols. PPMD sort of set the pace for these patient-led guidances and did a remarkable job of -- we had over 80 people involved in developing that draft guidance and that is -- as others have said, maybe beyond the capabilities of some organization and

maybe there aren't 80 people studying a particular condition especially in the rare diseases.

So what would the right consortia look like? Does it have to be all of the patient organizations in the space coming together? Would a single industry sponsor be acceptable or would FDA be looking for that industry participation to be spread among several companies?

How could academics be involved when, you know, that may be outside of what their purview is to understand what regulatory guidance looks like?

So I think some, maybe for setting of what's the minimum expected set of participants and then it can build from there, but to give people an idea of what they're shooting for would be really helpful.

MS. CHALASANI: Sure, thank you, Anne and then Marc.

MS. PARISER: Yeah and in addition to that I think also the "why" is important. I think we -- we heard that several times earlier this afternoon and again from this panel. We have a tremendous variety of diseases -- there's about 7,000 or so different

diseases that have been described and they're all various places along the spectrum of how well they're understood or -- or how organized they are.

So I think it's very important to everybody -- you have to take a very close look at where you are. Some of the diseases are very well described. Duchenne Muscular Dystrophy -- there's been a lot of work there.

There's a lot of rare diseases in particular, where we really are starting out. So what you're going to be collecting and the level of complexity can be very, very different but it can still be tremendously useful. For example, we heard a lot about natural history studies. Well maybe we're not quite ready for that.

One of the first organizing activities is -- is a registry. A registry is a very broad term, it's just really almost any data collection. But a communication registry is often a place to start and that can be of tremendous utility.

Now this may not be something you'd submit in a guidance to FDA, but that could form the start of -- of organizing your research plan. It could put you in

touch with the pharmaceutical industry who may not want to embark on a clinical development program if they don't think they can enroll a trial.

But if you're able to unite the community like this -- that could be a tremendous help in moving things forward. So, so I'll go back to what I was saying before -- look around very carefully. There are consortia that exist.

We have a rare disease clinical research network that has corrected longitude and observational data. Some of them are 15 years long. Now, not all of them have that but there may be something that already exists -- is it something you can build on?

Especially for rare diseases as it tends to be a small community, there aren't a lot of patients but there also are not a lot of researchers so you can often pull people together around one table to get started and to see where you are.

So I'd urge everybody to do that first and then decide what your first goal is that you're going to build on.

MS. CHALASANI: And I think Marc you wanted to

address this.

MR. BOUTIN: So first Anne, I think you're absolutely dead-on right. Whatever you do in the preamble of this guidance should encourage a self-assessment for any group that wants to do this about their organizational capacities and where the disease area is or we could get stuck in a lot of resources being spent inappropriately and a lot of submissions to FDA that may use a lot of FDA resources inappropriately.

I actually think most of your best work in the patient community is going to be submitted in other ways. And so making that point really, really clear and driving that home I think is critically important for the patient community to do that assessment and decide where they can have the greatest impact.

A couple of quick thoughts on this guidance -- can it be submitted in segments and sequentially? Thinking about that can it be made bite-size? Maybe some of the bites are submitted not as guidance but eventually a package comes together and becomes a guidance.

Recommending that to a lot of groups would make a lot of sense. When you have this information on your website, anything you can do to make it searchable -- and for organizations to say, “These are the 28 things that are critically important to me,” and to put that into the website so that when anything new gets put in, they’re notified to go back and look, will help make this a robust tool that can be functional not only for sponsors but for the patient community that may not realize that there are people in Europe and India and China working on the same issue.

MS. CHALASANI: Several hands, I’ll go to Annie?

MS. KENNEDY: So we -- as has been referenced, we did develop guidance for industry and the “why” was because we wanted to accelerate therapy development in the Duchenne space.

We had developed and funded research. We had several natural history studies. We had funded so many animal models we referred to it as the Duchenne zoo. And we wanted to bring all the stakeholders together and really look at our -- look at the space, assess the

space, and understand what we knew and bring it together before the FDA.

So, but I think it's important to say that that was not a guidance around patient preferences and patient experience data. There was a section about patient preferences because we had begun to embark on patient preference studies so we analyzed the methodologies that we had at that time been using in our community and talked about benefit risk assessment in Duchenne at that time.

And we also talked about what we called the imperatives which was from the perspective of our Community Advisory Board -- what was really important for our community to ensure that regulators understood about Duchenne.

So that was what was in the community-led guidance that went before the FDA. That was probably considered to be sort of a lightning-pace process. It took 6 months for that to come together in 7 work groups of over 80 individuals and stakeholders which included academics and industry and researchers and the patient community.

And we invited all of the Duchenne organizations and individuals in the Duchenne space that wanted to be a part of it. So convening the community was really incredibly important.

But again, that wasn't related to focus on patient experience data as we defined the clutch and the patient experience data. We have been collecting patient preferences, we have specific registry data and peer Ode's that are in development in Duchenne and we have been working to bring those into the FDA and publish those and work in collaboration with the relevant centers of the FDA to bring those in to the FDA.

And we also worked with bio in collaboration to develop a document and published it called, Key to Considerations in Developing and Integrating Patient Perspectives and Drug Development.

We used Duchenne as a case study but we looked at other communities that were also doing this work to look at what models and methodologies and what their experiences were in integrating patient perspectives throughout the drug development lifecycle, and again

talked to FDA around what were the considerations that were important to FDA, what were the time points where that data should come into the agency, and talked to industry about those same things.

So we think that there are some of these other models out there but guidance is a huge undertaking and so we're not saying, don't do it. But I think from our perspective we haven't seen guidance as the vehicle to bring patient experience data in -- that to us is needed to be a little bit more of an agile, iterative process.

MS. CHALASANI: Sure, Annie, while you're on the mic. Just since you're one of the folks on the table that's been through this process I mean, 6 months is already very efficient actually. But if answers to this were out there for these questions would that -- would that be helpful or are there still some key questions?

MS. KENNEDY: Oh, absolutely.

MS. CHALASANI: I mean answers are always helpful. I mean the last panel from the FDA is gold.

MS. KENNEDY: That kind of information is

always helpful. The one thing I worry about though with -- the one thing I worry about is if you put out a list to stakeholders to say these are the kinds of things we want to see in guidance.

You have to be very careful that it's not interpreted as, "We want you to do guidance on these things."

MS. CHALASANI: Yes, great.

MS. KENNEDY: I think I liked when Jeff said, air quotes around that for -- you need to make sure that it's not seen as a sort of edict.

MS. CHALASANI: Right --

MS. KENNEDY: That you need to be generating guidance for us and that that is the preferred method of communication with the FDA at this point.

MS. CHALASANI: Correct, and I think that's what we were really trying to get at with that sub-question underneath saying, "If you don't want to submit it as proposed draft guidance," -- even if it is that information that we talked about in Session I -- what are those other formats, but we really need to, apparently, highlight them and communicate them and

find other ways to get that message across, okay. Paul, I think I wanted to give you an opportunity as well.

MR. MELMEYER: Yeah, I wanted to build-off a couple of the points already made -- this is why we also need to be very careful with the case study model if FDA was to put forward a case study and let's say it was -- PPND's process or some of the other guidances that have been submitted to FDA.

I can imagine the vast majority of patient organizations within our space would say you know, "Holy Cow, I couldn't do that within 6 years let alone 6 months, so I'm just going to walk away from this and not worry about it."

So if we were to go forward with a case study model -- there would have to be a variety of case studies that fit a variety of different resources that patient organizations could put into the process.

I think it's also important to ask for whom is this data being generated for. I would imagine for many patient organizations who would be introduced to this process they may think, okay so, you know, we're

submitting this draft guidance to FDA so this data is specifically for FDA.

But in actuality this data may be most useful to industry as they are developing therapies for their specific diseases so that must be a point that is quite clear to patient organizations as they're thinking through what data should we be collecting in order to participate within this process.

And one final point, patient organizations within our space have to get particularly creative in order to get things done -- just due to very small resources and not resources that go around within rare disease research and patient advocacy.

And for this reason, many patient organizations that represent different diseases that are kind of within the same space oftentimes partner with each other on projects. We see this oftentimes within research consortiums and other avenues.

And so if there's an opportunity for patient organizations that technically represent different diseases but perhaps are all within inborn errors of metabolism or some other kind of subsets of rare

diseases.

If there's a way that they could partner together on collecting this data and putting forward a draft guidance, it would still be valuable to FDA, it would still be valuable to industry -- that should be well noted by FDA within its draft guidance.

MS. CHALASANI: Thank you Paul. Just really quickly going back to your case studies and examples on how it would be really helpful to have a range -- that's really a call of action to everyone in this room and on the web and other folks as well.

We have a public docket that's open I think until May 18th. If you could send us the resources and the examples, that would be very, very helpful. Earlier rather than later -- we have a very tight deadline for drafting this guidance, but that would be really helpful, Jeff?

MR. ALLEN: Just to add one thing and I don't mean to keep harping on the early interaction but I think it's really important in terms of determining the scope.

FDA uses guidance documents to communicate the

agency's positions on a variety of things and that's different than submitting data that would be valuable for FDA processes or for things that they may want to consider.

We also were involved with drafting a guidance document a number of years ago -- I think it took us more like 10 or 11 months, but I think what was important about that and the area that we were looking at was -- was multi-drug combinations for -- for two or more novel drugs for use in combinations that were otherwise unapproved.

And this was an issue that the oncology community was sort of -- had the foresight to see that this was the future for cancer treatment and a perceived barrier.

And we could have very easily just pursued the exact same publication that laid out a couple different clinical development programs that could be followed and that could have been informative as a publication.

And I think the reason that it became of interest to FDA was that the FDA was frankly sort of being identified as a barrier for novel, novel drug

combinations and I think this was a good venue for the agency to put forth their thinking in saying well here's the types of information that we could suggest to clinical researchers on how to produce and ways that would be acceptable from our vantage point and advice that we would give you, so it was of interest to them.

The second point was this wasn't unique to oncology as much as some of our efforts were focused on that, one of the charges from the agency were yeah look -- look more broadly.

So we brought in the infectious diseases community that had frankly more experience than the oncology community in multi-drug combinations. And the ultimate guidance document that the agency put forth was not specific to any of those diseases. There were some things that needed to be addressed in there to be specific as necessary.

But it was meant to be as encompassing as possible. But you know my point is I think that it would be important very early on to distinguish are these topic areas things where the FDA could lay out the agency's position on certain things versus ways in

which the external community can provide experience and information back to the FDA for those -- for their use, because I think those are different things.

And early is really important. I would only imagine that -- that if any individual within the FDA thought they themselves wanted to pursue some sort of guidance document they would talk with their colleagues and follow a procedure rather than drafting it and submitting it to, you know, the center director or whatever the case may be, you know, so it would be very important from the same standpoint I think for external groups to do the same.

MS. CHALASANI: Thank you Jeff. I think along the lines of communicating FDA communication, kind of, really going to that fourth goal at point about what will happen after stakeholders submit a draft guidance related to PED to the FDA.

So I'd really like our panelist's input on how can FDA manage expectations and really keep stakeholders informed on the practical considerations that Keith kind of touched upon earlier.

You know, there may be things that we just

can’t share. So what -- what are some of your thoughts on that? Like how can FDA manage expectations, what’s realistic? That’s Kim -- are you nodding your head or Annie?

MS. MCCLEARY: I was just going to say that you know some -- and it kind of goes to Jeff’s point about there should be a dialogue that proceeds submission of guidance so that you are somewhat confident that this is hitting at a time when FDA is ready to think about what its position on a particular disease area might be.

I mean otherwise you might be just submitting it and this kind of a “thanks for sharing” opportunity, or you get crickets because there isn’t really any perceived need within the agency to clarify something that they don’t have an urgency to act on.

So I think the response is going to be somewhat dictated by how well you’ve matched what you’re doing to what FDA’s needs are. Ultimately, I think as Paul said, the real audience for this might be industry but if, you know, we don’t want to use the FDA as a pass-through for every bit of information we want

to communicate to industry -- that's not a terribly efficient use of limited resources here, so.

MS. CHALASANI: We're happy to be facilitators but we do have day jobs, Marc and then Annie, sorry.

MR. BOUTIN: Even in our conversation here I think we're lending the potential audiences and I think we have to be disciplined about what is the audience and what is the purpose. You know, again I'll go with Jeff's air quotes, this really isn't a guidance per se.

In many respects it's very, very different and I think a lot of patient organizations perceive this as an opportunity to distribute information to a variety of audiences and there's a lot of value in that because there is no place to do that effectively currently.

If this is really going to be a guidance that is informing FDA's thinking, it becomes much more narrow. And to your bullet here -- the fourth bullet -- having clarity on exactly what the process and the timelines are are critical, but if this is the point of managing expectations we're too late.

So being very clear on what the purpose for this is because I'm hearing two different extremes

here. And it could be both, but being very clear what it is and then when a patient organization starts to consider this I think there's a lot of soul searching they have to do to figure out if this is the right pathway.

And there can be some opportunities to match expectations there. But the expectations are going to be set at the very, very beginning. If we're waiting to this point, we probably waste a lot of resources.

MS. CHALASANI: Sure, so what I'm hearing is the fourth bullet point should be the first or like right after the first one, almost, Annie?

MS. KENNEDY: I guess the -- a couple of things that came up make me think that this process is cumbersome, right? So, we're talking about there could be multiple stakeholders that are involved in developing the guidance and my understanding is that FDA doesn't necessarily -- if you have multiple stakeholders developing a guidance, then there's not necessarily one point of contact so that means that FDA may need to develop a process for identifying one point of contract that if there is going to be some type of

communication back and forth about the process, that there's an agreement on what organization -- which organization that is or who that's going to be if that's representative and then disseminates the information -- so that would be a new process that would need to be established potentially.

And then another question that's come up -- came up around our guidance is that we had submitted a community-led guidance and then FDA broke into docket for that to be submitted and then FDA developed a DAIS draft guidance for industry in Duchenne and those were two different documents -- so FDA's guidance looked more like an empty egg guidance and then there was a community-led guidance and both were very well-done, robust, scientific documents but they were different from one another.

And so there was a question of how do those relate to one another, link to one another, refer to one another? And I would imagine that something similar will come up here and so there needs to be a process for acknowledging that and setting expectations around that so that the community and industry know

what to do with that.

And then related to that, if then the community were to update their version of the guidance at some point -- and especially related to patient experience data, I would assume that gets updated fairly regularly. How does the one get updated and linked to the other, et cetera or does one sunset?

So just some questions or considerations around that.

MS. CHALASANI: I think that's really helpful, Anne?

MS. PARISER: So in a different -- in addition to the use cases that you talked about which probably need to be at very different stages, very mature research on beginning stage.

Perhaps something like a decision tree or pointing people in the direction of -- I have this amount of data. It might help you identify where the gaps are and where you need to then -- what should be your next step. This may or may not lead to a guidance but as Theresa's talk had a lot of other directions this could be put to, it might be helpful.

If I have a lot of information on clinical symptoms -- well maybe your next step is you want to start developing an outcome measure.

MS. CHALASANI: Thank you Anne, Mary Jo, sure?

MS. STROBEL: Just to build on that. I think any guidance issued would need to be very simple language that could be easily understood by a patient, an advocate, a lay person. I would say most -- many, if not most, advocacy organizations that are serving those for rare diseases are started at the kitchen table and they are run by those who may have little or no medical background.

So it would be really important that any guidance is written and presented in a way that can really be easily understood. Very clear sections would be helpful as they're navigating -- planning implementation, submission, post-submission, very simplified so it's not so cumbersome, or intimidating when they are embarking or assessing how to move forward with that.

You had asked earlier if templates would be helpful and I would say yes. Having sample questions

structured in a way that's going to help draw out what is the most meaningful data for all parties is really helpful, again thinking about who is accessing this.

The various channels that that information can be captured -- again scalable -- what one group might have a budget to -- and the support to host an in-person meeting to bring the patients together, there are many in the space that maybe they're only patient engagement.

They've got the patient engagement but maybe it's through social media and how would we -- how would we address that and what are ways that that could be harnessed and used and submitted?

MS. CHALASANI: I think Paul and then Bray.

MR. MELMEYER: Yeah, just to build off that even further. In regards to managing expectations as Marc was saying earlier that, you know, needs to be addressed before the guidance is even really considered.

And to have an open line of communication between patient organizations or those who could be pursuing these opportunities and those at FDA from the

very start is really key to insuring that patient organizations are choosing the right way forward.

Perhaps they just raised $10,000 they want to spend it on something -- is it best to start a registry or should I look into a guidance or should I hold a scientific meeting with FDA. That can't really be reflected in the guidance on guidance because that is unique to that patient organization specifically and that could be covered within, you know, an hour-long conversation with FDA.

So ensuring within the guidance on guidance that there is something to day that for your unique circumstances, you're considering how to best engage with FDA, how to contribute your patient-communities' perspectives, you know -- this is who you talk to, this is who you should be reaching out to -- to have that conversation.

MS. CHALASANI: Sure, I think that goes along with the earlier idea of a decision tree or Marc you mentioned a framework kind of along those lines, Bray?

MS. PATRICK-LAKE: So I guess I want to go ahead and just have the hard conversation about you

know what about when things go wrong? So right now, we've got the early adapters and the people that are open to this and pretty good at it but we know that not every patient group is the same, not every industry sponsor is the same and not every FDA reviewer or division head is the same and their thinking.

So I wonder what happens when people submit. So we're saying you shouldn't really be submitting unless you've already kind of come to agreement that there's a need. But we also heard FDA sometimes doesn't think there's a need when patient groups think there's a need.

So how do we work through, you know, is it just a -- you get an email back that says thank you but no thank you. Thank you, what you submitted we don't find rigorous, thank you, you don't have the right stakeholders -- you know what -- what do people get back to choose for or do you get something back that says, you know, this is what, you know, how you move forward from here or what we really need or you know, can we meet because we're discordant.

I mean I just -- I want to have a little more

conversation about what that looks like.

MS. CHALASANI: Sure and I think I'm going to turn that question back to our panelists -- what would be useful in that circumstance, Anne?

MS. PARISER: Well I mean FDA I suppose is not the only player otherwise we're here for the guidance -- but not the only player. So chances are if -- if there's discordance I'm thinking it's probably premature so you're probably going to need to go seek additional help.

So again, NIH, the experts in the disease, other patient groups -- that would probably be the next step in seeking some help.

MS. CHALASANI: Paul?

MR. MELMEYER: And if there is discordance hopefully FDA has a suggestion on what to do instead. Perhaps they do disagree that it should be a guidance that would be developed but you instead, in your specific situation, you know, patient organization next -- you should be doing this instead and therefore FDA can still have a proactive productive suggestion for the patient community to pursue that would still be

beneficial for drug development within their space.

MS. CHALASANI: Annie and then Marc.

MS. KENNEDY: So perhaps the process looks -- I mean to Jeff's point earlier, it looks similar to the PFDD meeting process where what you're asking for initially is an LOI right? So, and a brief description of the effort and who you look to involve and the identified need, and -- and then it's the beginning of a conversation.

So you haven't gotten so far down the path where there's been an investment of time and resources that it's actually a great opportunity to begin a relationship with the right people at FDA to really help you do that assessment of your community and what you're working towards.

And so it maybe at that point where you're invited in to say, "Absolutely, let's talk about this, and flush this out a little bit," and put you in touch with people who that can help you navigate the next steps.

Or it can be you know what -- the next steps before you get to this might this this and let's help

point you in the direction of those kinds of resources.

MS. CHALASANI: I think that's a really good idea, Marc and then Kim?

MR. BOUTIN: So Annie we're channeling exactly the same idea. You might consider a requirement that you register an intent to pursue a guidance first to start that conversation.

My biggest concern here, I'll be really frank, is a lot of resources are going to get wasted developing guidances or diseases where the disease either is not ready or the organization is not ready. And there are too few resources in the patient advocacy community to allow that to happen.

So I have a real concern here. What -- the feed that I'm picking up is that your opportunity to collect hopefully high-quality information and to curate that and to make it public -- short of a guidance, is really what the patient community was looking for.

And to really beef that up and to connect it to the guidance might be relevant. But it's probably going to be relevant for a small percentage of -- of

disease areas where people are ready. And when they're ready we absolutely want to encourage that.

But many in our world are going to need to get ready. So it feels like the guidance on guidance is sort of being over-weighted compared to the other opportunity to share information through this web portal.

And I think we may want to think about how we reverse that and communicate that effectively to communities so that we can use that portable -- portal to get great information out there that builds on our body of knowledge, curated appropriately, make it searchable, get it to the relevant parties, encourage collaboration and then when the time is right let's move to the guidance.

MS. CHALASANI: Kim, if you want to build off of that?

MS. MCCLEARY: Yeah, I think that's -- that's really important and one thing I'm thinking about sitting here is in some diseases where the kind of standard of care is -- revolves around drugs, it's more -- maybe more straightforward of who you work with but

so many of the conditions there's interplay between biologics and drugs and devices.

And we -- we heard a lot in the PFDD meeting series about supplemental oxygen and ventilation machines and it's not clear like maybe it could be diagnostics, or diagnostics paired with treatments and how would a patient community know who to seek out and how to involve other centers in that work and the timing of when it makes the most sense as well. I think that's important too.

That letter of intent process might help clarify who the internal partners within FDA might need to be.

MS. CHALASANI: Just to provide context for externally-led patient focus drug development meetings, our process starts with asking groups that are interested in hosting a meeting to submit a letter of intent to our office so that we can review and then work with them to help support them in any way.

I do want to leave some time for the audience facilitated discussion so I'm going to turn to my panelists and just ask if there's any final concluding

remarks or anything you'd like to say, Kim?

MS. MCCLEARY: Another thought that came up is and using Jeff's air quotes -- the guidance, you know, even in the best of circumstances it takes six months, probably longer than that if you're mortals.

There are certain circumstances though like potentially, you know, how could a patient or an external stakeholder submit information for an Adcom meeting where there is potentially patient experience data that could help inform a particular product decision even if that data wasn't collected, you know, about a specific product but just helping understand what the trade-offs are?

And that may be a shorter timeline given PDUFA timelines of when the deed is immediate, how could there be maybe some accelerated pathways and there may be PFDD meetings externally led where other communities have information that they feel could be important to bring to bear but they aren't specifically involved in that meeting, so just a couple of very specific instances.

MS. CHALASANI: Sure and I think our external

resources webpage that Pujita presented on may be working in that direction and that it's entitled to a resources -- resource for external stakeholders as well as FDA staff, for example, preparing for an advisory committee meeting. Any other -- Bray?

MS. PATRICK-LAKE: I just want to make one more request. On the cover page I thought it was great. A lot of good information but authors and collaborations -- I was wondering if you could add roles? I think it's important to really understand --

MS. CHALASANI: Sure.

MS. PATRICK-LAKE: What contributions are -- I know it said financial, but I think, you know, is it a patient group that got bolted on and they're you know, not really driving the effort?

I think we want to elicit that and understand who contributed.

MS. CHALASANI: Sure, I think that's really helpful feedback, thank you, Paul?

MR. MELEYERS: Yeah and to build on that we know that patient organizations are always very cautious in approaching relationships with industry so

they'll want to know to what extent industry -- regulated industry, should be involved within generation of this data so that they're -- they can ensure that whatever data they generate will be looked at by FDA in looking in the light that they'd like it to be looked at.

MS. CHALASANI: Okay, helpful, thank you, what else Marc?

MR. BOUTIN: So, really, I think everything is Bray -- I'm glad you mentioned that. I had made a note about that and forgot about it. I think it's critical to say that it's okay for it to be funded, but there'd need to be appropriate guardrails on how that works, guaranteed independence, mission-related context for the patient organizations.

So not just simply asking where the money comes from because that will lead us to a certain set of conclusions but understand where the money came from being completely transparent about it and also what governance independent mission drive was there? And there are ways to get that that.

And organizations should be expected to

communicate that.

MS. CHALASANI: Okay, great. Unless there's any final thoughts, I am going to open the floor for the audience facilitated discussion. So a lot of the same questions that I've been asking the panelists here.

What would be helpful for FDA to address in our guidance on guidance, now that we're using air quotes? We do have few mic runners -- a couple of them that are going to be walking around so please just raise your hand and they'll bring a mic to you. I see Dr. Roberts in the back over there.

MR. ROBERTS: Thank you, thank you for a great discussion today. I'm Steve Roberts of the Tuberous Sclerosis Alliance, and I just wanted to add a voice to -- to some of the groups that are close to ready for guidance.

That the guidance for guidance, maybe with a capital "G" is important to some of the -- some of the groups, so while it doesn't work for everybody, I just didn't want to leave the discussion thinking we need to, you know, take it really, really down because I

think I and maybe some others wouldn't be here if it was a discussion about how to improve a -- a website and sharing.

We're really interested in taking it to the next level so I appreciate all the input on, on doing that to help us do it the best way we can.

MS. CHALASANI: Sure, I see a hand.

MS. KENNEDY: Can I just make one remark though. I think to that end and I mean disagree with me if you disagree. This panel blew past the guardrails of the statutory language where we opened because the statutory language talks about how a person seeking to develop incident proposed draft guidance relating to patient experience data for consideration by the Secretary.

And we're really talking about submitting guidance for guidance so I think probably a lot of us who have submitted guidance didn't just cover patient experience data, but really looked at our ecosystem around the scientific data, the natural history data and brought it all together and I think that's how we've been -- we've been using the big G and not just

looking at what patient experience data we have to bring in.

So I think that's important to clarify though today because we aren't just looking at how to bring patient experience data forward, but what's new about our disease condition and how to bring that forward.

MS. CHALASANI: Sara, I think you had --

MS. BRYSON: Okay, thank you first of all. This was wonderful. I'm Dyan Bryson, I'm with Inspired Health Strategies. And what we do is work with pharmaceutical companies to help them become more patient centered and help them develop strategies to improve health outcomes as well as the bottom line.

And what I saw in this opportunity originally it sounds like might not be the original intent, but it could be an opportunity. Many companies really have developed initiatives that had been effective but the learning doesn't take place and the projects aren't replicated because the education leaves the organization or that person leaves that role that they were in.

And there's nowhere to put all of these

programs that had been effective that pharma can learn from which is seems like this is part of the intent and isn't it possible for pharmaceutical companies to submit -- and not everyone has good ones, but for pharmaceutical companies or those of us who work with them to submit initiatives that we have seen to be effective?

MS. CHALASANI: Pujita, feel free to correct me if I'm wrong but I do think the answer and FAQ's for external resources website -- the "who" and in statute also says the "who" and it really can be any stakeholders, so I think that's the answer to your question, okay I'm getting nods from my left here, other folks, oh in the back?

UNKNOWN SPEAKER: Yes, since you're specific about finding guidance from guidance, my thoughts about it is -- guidance from guidance, probably really should be most importantly to connect with the other -- the other regulations in European countries.

They have those entities, all the nations in Australia, there are so many other continents haven't targeted it because they must already have such

(inaudible). They may ahead in this game so this is my thoughts.

Have you tried communicating with them?

MS. CHALASANI: I don't know -- I don't know the answer to your question but we can take it back. I do know that one of our other commitments is a repository that we have to develop and that's something -- it may be the external resources webpage that we presented that may grow into that.

It may be a separate effort to be decided. We have a little bit more time on that. But we do envision it to be disease specific and it may be broader than just information that's collected for the United States population so going towards that facilitation and collaboration and consortia, all those other themes that we heard.

Hopefully that kind of answers a little bit of your question. Other folks -- I wanted to ask about that sorry?

MS. PATRICK-LAKE: So I know on one of the webpages it said, "See who else is working in the space." Is there like a specific direction for

landscape analysis?

MS. CHALASANI: Sure, sorry I missed the beginning of that question, Bray, would you mind re-stating?

MS. PATRICK-LAKE: I'm just limited -- I know that on one of the resources it was saying that you should identify all the other people working in the space but it didn't say like landscape analysis and I don't know U.S. specific, I think, was his question versus global --

MS. CHALASANI: There could be something --

MS. PATRICK-LAKE: But there was something about who the other collaborators were.

MS. CHALASANI: Sure, we can take that back and consider that, yes?

MR. MELMEYER: And I do believe there is a patient engagement cluster between FDA and EMA -- perhaps that could be an opportunity for the cluster to talk about international collaboration on this?

MS. CHALASANI: Yeah, that's a really great suggestion, thank you.

MR. MELMEYER: Thanks.

MR. BAKER: I'm Jim Baker, I'm representing FARE, the Food Allergy Foundation. I'm an allergist. I've been involved in drug development my entire career. And we're almost the opposite of many of the organizations here in that we have an outbreak of a disease that has multiple causes and the impact is very different.

We have both pediatric and adult and we have people who have an allergy to something like peanut which is avoidable as compared to milk and egg which make their lives much more difficult.

Obviously, we are not ready to go to guidance yet and I think in particular for problems like this that are emerging, we don't have any therapies that are approved yet.

This is a very important thing. So the concept of providing input to an Adcom or something in another way that could have an impact for our population is something that's very important and I don't want to get lost in the fact that we outweigh the (inaudible).

MS. CHALASANI: So really providing some

communication on the range of opportunities, other folks -- I see a hand right there.

MS. EISENHOWER: Hi, thanks, this has been very helpful. My name is Jessica Eisenhower, I'm General Counsel for a company called Corona, we're collecting longitudinal observational data for -- since 2001 in autoimmune diseases.

And I sort of came into this thinking we were going to be talking a little bit about how industry could utilize existing registries and I was very pleased to see all of the patient organizations involved. And one of the questions for the FDA and other may have been mentioned a little bit is -- is the expectation that patient organizations will collaborate with registries or other companies or whatnot that Anne had sort of mentioned that already have methodologies and designs in place?

Are the patient organizations expected to work and collaborate with registries or and would the expectation of desire of the FDA or is the FDA really interested also in sort of the expertise that a company like Corona and others can bring to the table even

though it might not be a patient organization because -- and I'm also a little bit unclear as to whether the FDA is asking for the PD rated information directly from patient organizations or whether they are expecting that information to come initially from the organizations and registries but be reported by industry -- so?

MS. CHALASANI: So really clearly stating or communicating the "who" that I think we're talking about would be really helpful in this guidance.

MS. SANTIAGO: Hi, I'm Kristen Santiago with the Cancer Support Community and I do want to just touch on the focus of patient experience data and the expansion of the definition to include psychosocial and physical impacts of an agent.

This is something that our organization is really interested in understanding the full patient experience beyond just what -- how the drug works so trade-offs to work/life balance -- things like that.

And I think that there's an opportunity going forward with patient focused drugs about when to either in the checklist that's used when you're capturing, you

know, what patient experienced data was submitted to really outline was there a psychosocial data submitted.

And then also potentially help define some of the -- the psychosocial impacts could be that people can submit in their guidance or other forms of sharing that information, so thank you.

MS. CHALASANI: Thank you, other -- other comments or questions that we should address?

MR. HO: Hi, I'm Calvin Ho from the Tuberous Sclerosis Alliance. I wanted to build on the second to last question and also on Anne and Paul's opening remarks. So we've discussed that a lot of patient advocacy groups don't really have the resources or the expertise to collect very good data, but we need very good data in order to make good decisions because bad data is at best, useless, and at worst very misleading.

So I was wondering if we could brainstorm a bit about how we can help patient advocacy groups, you know, collect data that will be useful to FDA?

MS. CHALASANI: Sure, I think Theresa outlined some of the other guidances that are part of the PFDD series -- really those guidances 1 through 4, so those

methodological guidances and I see that those are going to be targeted towards the methodology to really collect representing and robust data -- that's took for purpose, other comments, yeah?

MS. KENNEDY: The one thing I do want to say is that I do want to caution people that it doesn't actually -- it doesn't cost a lot of money to start collecting resources if you have the ability to reach patients.

And that many of our organizations, all -- most of our organizations started with almost nothing and one or two parents that cared and found other parents, and long before social media.

So now in the day and age of social media, you can convene a community much quicker and there is a resource now through NCATS called the tool kit, the NIH tool kit and I think Anne referenced it a few minutes ago -- where the community came together to identify across the drug development lifecycle where all of these resources were so that patient organizations didn't have to reinvent the wheel but could do a quick swat assessment and needs assessment to figure out

where your community was in the drug development lifecycle, where the resources you needed to build where.

And then plug into those tools and resources that had been mapped out and invented before you came along so that you could benefit from others who come before you and didn't have to start from scratch. And those this is where industry and patient groups and government -- federal partners came together and developed that tool kit together.

It was just launched a few months ago. So for those streaming and those in the room, don't feel like you're starting at zero because anybody can convene and build a community and do any of the things we've been talking about today and you don't have to start from scratch.

The templates have been pushed out and shared and we all publish this so that people can come behind us.

MS. PARISER: Yeah, I would agree and don't sell yourself short. You can do an awful lot with a little and this is especially true in diseases for --

that are not -- that don't have a lot of research going on or a lot of information right now.

A little bit of information can be a surprisingly big push to a research agenda. So, you know, take a look at the resources that exist, look at what people have done -- even a small but thorough good quality data collection can be extremely informative.

MS. CHALASANI: Thank you. I have permission to go five minutes over so I'm going to take one or two and that's it. Sorry, but we have the public docket so.

INAUDIBLE NAME: Randy (inaudible) with the (inaudible) Research Foundation so I'm familiar with the rare disease community. Marc's comment -- and what I'm hearing today is what I've heard for the past 15 years. You know, patient centricity, FDA guidance, I think disease specific guidance, you know, is a good idea.

But at the end of the day in order for this to work we need to have a way that the patients and regulators and the sponsors are at the table, literally, when these kinds of final decisions are

being made as far as what's acceptable risk -- what's success in an outcome.

So the guidance is not binding patient engagement of companies is advice sponsors or you know, doing applications, but we can do all the guidance we want but if we don't have a point where people have to come together during the process, it's hard to see everyone adopting this in any kind of a reasonable timeframe.

MS. CHALASANI: Okay, thank you. Okay, I think with that we're going wrap Session II. I want to thank all my distinguished panelists up here, thank you so much for your expertise and your insights and everyone in the audience as well.

And now I'd like to invite Pujita Vaidya for the open public comment.

MS. VAIDYA: Thank you Meghana and all of our panelists. So this wraps up our panel session. I know some folks have meetings to run to at exactly 5 o'clock so I'm going to try to keep this short.

This is the open public comment session so if you're not -- if you don't know what the purpose is for

this -- it's really to allow an opportunity for those who have not had a chance to speak to provide their comments. We ask that you, during the -- during the process we ask that you -- encourage you to note any financial interests that are related to your comment and if you do not have such interest you may state that as well.

So we actually have 1, 2, 3, 4, 5 -- 5 people signed up for this although I do know some of you have already spoken so you may -- I don't know if you want to take your names off, but let's jump to it really quickly. First, we have Campbell Hutton from JDRF. If you could find the mic -- okay great, and you have two minutes for this, thank you.

MS. HUTTON: Good afternoon, I am Campbell Hutton as you just said, Senior Director of Regulatory Affairs for JDRF and I have no financial interest to disclose.

JDRF is the leading charitable organization funding type 1 diabetes research with a mission to accelerate life-changing breakthroughs to cure, prevent and treat the disease.

It was founded by parents of children with type 1 diabetes and is led by a Board of people with personal connections to the disease.

Type 1 diabetes or T1D is an autoimmune disease in which insulin-producing cells in the pancreas are destroyed by the body's immune system. T1D can be diagnosed at any age. Its causes are not fully known and there is currently no cure.

People with T1D must take insulin multiple times a day to survive and given the shortcomings of current treatment, typically spend many hours a day with blood sugar too high or too low which can result in serious complications and medical emergencies.

JDRF strongly supports FDA's convening of this public meeting and the overall effort on patient focused drug development. We applaud the resources and energy the agency has put into fully integrating the patient voice into decision-making.

12 years ago, JDRF embarked on an effort to work collaborative with the agency to develop a pathway for regulation of novel, complex medical devices called artificial pancreas systems.

Through this collaboration a guidance was developed and within a decade our patients saw the first artificial pancreas system approved and available in the U.S. These tools are now revolutionizing care for people with T1D.

And we're thrilled to be able to engage again with the agency on this -- on the very important focus of this meeting -- patient experience data. We have found that a multi-dimensional approach to patient-focused drug development that incorporates patient experience, scientific evidence and clinical knowledge to develop a flexible, safe and effective regulatory pathway can improve therapeutic options and health outcomes for people with T1D.

Hemoglobin A1C is the accepted surrogate efficacy outcome for T1D. Advances in technology have now made it feasible to measure additional outcomes, but these have not been consistently defined or used.

Over the past two and ½ years, JDRF and the leading T1D clinical organizations and other research funders have come to consensus on the definitions for clinically meaningful outcomes beyond HBA1-C and the

consensus was published in diabetes care late last year.

A patient preference study is also being conducted to quantitatively understand how patients and caregivers value these outcomes. We look forward to continuing to work with the agency to incorporate the consensus of patients, clinicians and researchers into our refined regulatory pathway for T1D therapies so that the risks and benefits are fully considered and people with T1D can benefit from therapies that are truly clinically meaningful in their daily lives.

We greatly appreciate the opportunity to make these brief remarks to the agency today and look forward to continuing to work with you on all the elements we've highlighted, thank you.

MS. VAIDYA: Thank you Campbell, next we have Jack Mitchell from National Center for Health, and if you could please limit your response to two minutes please, thank you.

MR. MITCHELL: Good afternoon, thank you for the opportunity to speak. I'm Jack Mitchell, Director of Health Policy for the National Center for Health

Research.

We perform original health research, promote consumer oriented health policy and legislation and we focus on patient centered research and treatment. We do not accept any funding from any pharmaceutical or medical device company so I have no conflicts to report.

We thank FDA for convening this worthwhile workshop and we comment the agency for listening to patient advocacy groups and for elevating the profile of its patient affairs and engagement office -- a process now only a few months old.

However, patients who have been harmed by a medical product or have concerns about safety and efficacy issues, who are not represented by many of these patient advocacy groups often feel they are not always listened to by FDA.

They tell us that patients advocating for new treatments who are often affiliated with industry seems to get the bulk of FDA’s attention. More than 80% of the patient groups receive funding from some aspect of the medical industry.

And I'm not here to bash industry support of patient advocacy groups. It greatly and furthers the critical medical research in this area and it focuses the agency and the public's attention on these crucial medical issues, but it doesn't include all the patients out there -- many of whom we hear from.

These patients don't read the Federal Register, they don't know they're allowed to submit public comments to FDA, and they have no one representing them.

They often ask us is it worthwhile to come to a meeting like this at our own expense when we don't even know the morning of the meeting that we're going to be allowed to speak and if so, only for two minutes.

So these people deserve a voice at the table too, independent voices -- we're not affiliated with these groups and I'd like to advocate today for their presence and inclusion in the effort -- the very good, very worthwhile efforts you're making which we intend to cooperate with.

Also, I'm happy to hear that CDER and other centers are reforming the ways they do personal

meetings with patients because it's often hard for these independent patients to get in here and talk to somebody who can do more than listen to them.

And it shouldn't take a Congressional staff or an intervention by a public health organization to get these independent voices of patients in here to have people listen to them at FDA.

Doctor Gottlieb has made every effort as far as I can see to meet with patient groups and take on their point of view. I know he's done that because we've heard from those groups so we hope that the other ranking officials at FDA and the rest of you will take that as a cue and expand your efforts in that regard. And with that I thank you for allowing us to express our views.

MS. VAIDYA: Thank you so much Jack. Next, we have Kristin Santiago -- no okay, we're done -- great. James, sorry -- James Baker -- are you in the audience -- Food Allergy Research Group? Okay, and then finally Jessica Eisenhower? Okay, great, perfect. So that wraps up our OPC -- open public comment session. I will now turn it over to Theresa Mullin for closing

remarks.

MS. MULLIN: Thank you Pujita. Alright well this was a fantastic meeting for us. I mean I have to say I am so glad that we said, “Let’s ask people if they want to hear guidance be pro-related because it was extremely helpful as usual, to hear from people about what would be helpful for us to be putting in a guidance document.

So I think one of the big takeaways for us which is really helpful is that the guidance on guidance shouldn’t just focus heavily on guidance -- which is really what we wondered about that and then where do we go after that -- that was really helpful. The air quotes took a try seeing if they could figure out how to do that and see if our Reg Councils and our Chief Counsel’s Office will let us put air quotes around the guidance.

But the -- to talk -- maybe but my preliminary -- and we’ll get, you know, we’re recording this and we’ll go back and we’ve all taken notes on this but it sounds like one of the things we were hearing here is talk maybe first and foremost about that wider set of

needs for patient experience data and opportunities to -- to develop that kind of information and -- and that while we may not welcome something that didn't look like it should be a guidance as a guidance, but we really would always welcome that kind of information.

I think I've never heard of anybody say it's not extremely useful and helpful, but we could maybe try to provide a roadmap -- I was hearing a roadmap for external groups who may want to collaborate -- maybe working on their own, maybe collaborating with others with better -- you know the kinds of groups for example listed in the statutory definition.

Develop a roadmap and mention maybe a decision tree we could try, see what formats work to help think through what their disease area needs are, how -- to try to get a sense of what sort of the needs, what's already been done, what are they and their partners or collaborators able to do and what are they resourced to do?

And then really try to look from there what the opportunities are that might be a good fit for them. I mean I think we would not want to be too

prescriptive or algorithmic about this. I think we're too early in this whole undertaking to have algorithms and recipes that are all, you know, the best recipe you could have.

So I think we're not quite ready for that. It sounds like we should also consider if there are ways to get input from FDA without having -- admitting of every -- of every time we would like to pre-anticipate a lot of these questions in the guidance document -- that would be the point of it.

To try to lay out as much as possible in the document, but maybe there are times when it -- it would be really helpful to consult with or talk to somebody FDA about what you have in mind or, or if we know of other things but -- and we will be trying to put as much of that as we can to identify where -- where those resources are available.

I mean and Anne Pariser also mentioned the NCATS information that would be extremely helpful. I think we also want to make clear that we're not going to orchestrate what groups do, or we're not going to say your -- the ideal group has X, Y and Z on it --

that’s just not our job.

And I think what it would be, you know, that’s -- we think the best efforts will come forward from you looking around and seeing what’s possible and who you might, can and want to work with and that -- but we heard that there’s a concern that that kind of a -- groups be -- maybe if there’s something desirable there about a mix -- or you don’t have to do it.

One part is not responsible for it. Patients aren’t the only parties or who are supposed to be doing this -- that’s just -- so we make sure that that’s not conveyed because that certainly wouldn’t be our intention to convey that.

Try to be really clear, if we can, about who can submit to make sure groups understand we’re not looking for just a certain type of party to make submissions going back again to all those different types of organizations and stakeholders listed in the statute.

We were told to try to set the bar high and make sure the expectation and the desirability of meaningful engagement with patients is clear, including

to industry. I don't remember who coined this -- it might have been I heard this at a city meeting some years ago. I don't know but patient centered drug development as opposed to patient centered drug development and so we -- we're not interested in just getting the -- you know, the sort of the odor of patient involvement, we want the real thing.

And also, I think one thing that a good suggestion was to try to identify what kinds of roles in our cover page. If you have ideas about what would be a good couple of categories of rules and how they might be defined that would be -- make sense to you as people who might be putting information into those cover sheets and what kinds of governance there might be and descriptors that you think might be in simple definitions that you think would be meaningful to outside groups who would be submitting something to us.

We'd really welcome hearing that and getting that in the docket as well, as well as any other ideas. And I hope it's understood that we -- we always do webcasts for these meetings because we know people can't necessarily travel here.

And we've made that a practice in all the patient focused meetings because patients can't travel and a lot of people can't get here, not just because they don't have resources but they are physically unable sometimes or they can't leave home.

So I think that hopefully that a lot of these folks have been able to participate in the webcast today and we've made that a regular practice and submit information to the docket if they have ideas.

And so with that I thank you so much today. I can't tell you, this has been so helpful to us in moving forward with writing this air quotes -- guidance on guidance document and we'll be looking to get a draft of this done before the end of the fiscal year.

Of course, the federal fiscal year ends in September so that would be our -- our time frame for trying to aim to get out a draft guidance. Again, thank you so much and I hope that you're travels home are without any incident so with getting home today so thanks again for coming here today and being on the webcast.

CERTIFICATE OF NOTARY PUBLIC

I, KEVON CONGO, the officer before whom the foregoing proceeding was taken, do hereby certify that the proceedings were recorded by me and thereafter reduced to typewriting under my direction; that said proceedings are a true and accurate record to the best of my knowledge, skills, and ability; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this was taken; and, further, that I am not a relative or employee of any counsel or attorney employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

KEVON CONGO

Notary Public in and for the

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I, HELEN VENTURINI, do hereby certify that this transcript was prepared from audio to the best of my ability.

I am neither counsel for, related to, nor employed by any of the parties to this action, nor financially or otherwise interested in the outcome of this action.

Helen Venturini

03/29/2018

DATE HELEN VENTURINI

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