Patient Voice in Rare Disease Medical Product Development
Hybrid Public Meeting
October 16, 2026 | 1pm - 5pm (*eastern*)

Transcript

Welcome
Susan C. Winckler, RPh, Esq., CEO, Reagan-Udall Foundation for the FDA

Susan C. Winckler:

The [00:00:30] stinger was to help cue you all to take your seats because we're going to begin the meeting. I'm going to thank you for joining us, both in here and online, because our online audience is ready to go. We are thrilled to have you here for today's public meeting on the patient voice in rare disease medical product development. I'm Susan Winckler, and I serve as Chief Executive Officer at the Reagan-Udall Foundation [00:01:00] for the FDA. For those of you who are new to the foundation's work, we are the nonprofit, non-government organization created by Congress to help the FDA do more to protect and promote the public's health.

Today's meeting is part of that work, bringing together representatives from across sectors to explore the patient voice in rare disease medical product development, biologic, drug, and device. I'm going to ask my colleague here to mute this computer because that's the one that's providing the feedback. [00:01:30] And we want to hear the patient voice, not mine twice. But this is a meeting about where the patient voice is sought across the development timeline, its impact, and additional opportunities for patients to engage in the product development process. Insight from today's discussions will help inform recommendations for product developers and regulators to consider as they advance patient-centered approaches to their work. This is not a meeting about specific [00:02:00] regulatory applications or individual products. The foundation does not engage in regulatory decision making.

Now I have just a few housekeeping notes to cover. We're joined today by about 150 people here in the room and over 900 who are joining us virtually. Because of the size of the meeting, the virtual attendee cameras and microphones will remain off throughout the event. If you have a question and are attending virtually, please use the Zoom Q&A function to submit your question. For [00:02:30] those of you in person, write down your question and a staff member will get it to me. I will note, however, that I believe we have planned most of the conversation today, but do welcome your questions as you have the opportunity to submit them.

We are recording this event, and we'll post the recording and the transcript on the foundation's website next week. And the slides are already available on the event page. For those of you who are present in person, we ask that you [00:03:00] do not join the virtual transmission, but rather embrace the in-person interaction in the room.

So I'm going to give a quick overview of the agenda, but before that, I thank each of our speakers for investing their time in preparing for and delivering remarks today, and also thank our colleagues at FDA's Rare Disease Innovation Hub. We appreciate your partnership and support in planning this vital public meeting.

So let's quickly orient to our time together, and then I will do far less [00:03:30] talking and we will have much more engagement from those who have joined us. We will begin with opening remarks from Amy Comstock Rick, who leads the Rare Disease Innovation Hub, and we'll have a non-fireside chat with two of the Rare Disease Innovation Hub co-chairs to set the stage. Then we're going to hear from FDA staff directly to talk about existing mechanisms for engaging the patient voice into FDA opportunities. [00:04:00] We'll then turn to some case studies to hear about what folks can learn from successful interaction. We'll take a short break, and then we come back with a nine-person panel to help us think through the various opportunities to gather, strengthen, and feed back the patient voice in rare disease medical product development. And then we will close the day with a conversation with [00:04:30] our third Rare Disease Innovation Hub co-chair, Dr. Michelle Tarver.

So now that you understand our tour that we will be on for the next four hours, I am going to turn the podium over to Amy Comstock Rick, who is director of the Rare Disease Innovation Hub, where she serves as its primary external liaison, coordinating with stakeholders to implement its strategic agenda and foster collaboration across agencies. Is that all on your business card or just ... All right, [00:05:00] excellent. Come on up, Amy.

Opening Remarks

Amy Comstock Rick, JD, Director, Rare Disease Innovation Hub, FDA

Amy Comstock Rick:

Thank you. I should have said, "Wait, people have business cards still?" Thank you, Susan. And good afternoon, everyone. This is really a special day to have you here to talk about this, such an important topic. Actually, today is also the second anniversary of the Rare Disease Innovation Hub. On October 16th, 2024, [00:05:30] the Hub was launched in a meeting hosted by the Reagan-Udall Foundation to hear from the community about priorities for the new Rare Disease Innovation Hub. Today, as you see, we are partnering again with Reagan-Udall to address a priority that was frequently voiced two years ago and which remains a key priority today, engaging the patient voice across the rare disease medical product development pipeline.

Just a little bit about the last two years for the Hub. In the last two years, the Hub has [00:06:00] remained dedicated to our core mission to improve outcomes for rare disease patients with particular focus on the challenges within smaller populations by both internally serving as a point of collaboration and connectivity between FDA's medical product centers and externally by working with all stakeholders in the rare disease community, drug developers, foundations, disease organizations, academics, and of course patients, towards [00:06:30] achieving that core mission.

As a quick Hub recap, in the last two years, we have launched the RISE workshop series, which covers scientific challenges in the development of medical products for rare disease, launched the publication of FDA Rare Connections, an all-FDA quarterly newsletter that delivers rare disease news to the people to whom it matters the most, the rare disease community, enhance internal coordination, both formally

and informally. And I think you'll see quite a bit [00:07:00] of that in the next panel and with all three medical product centers represented today. We've sponsored FDA's annual Rare Disease Day, an event that has been going on for years and is now a Hub event designed specifically for patients to hear about how FDA is working for them every day.

And just Wednesday, we announced that the Hub, in partnership with the commissioner's office, CDER, the Drug Evaluation and Research Center, and the Center [00:07:30] for Biologics Evaluation and Research, an initiative, the Rare Disease Framework Initiative, to develop a new framework for the development and review of rare disease therapies, including a new fit-for-purpose regulatory approach to rare disease and biologic development, earlier inclusion of the patient voice, enhanced engagement with external experts, particularly on the very small rare diseases, and a fresh look at CMC requirements in certain [00:08:00] particularly difficult circumstances.

But today's meeting is not just about the framework announcement, but the broader inclusion of the patient voice in all stages of medical product development and by all relevant parties. And I'm confident Susan will keep us on track about that.

I really look forward to the discussion, and we'll turn now to thank our two co-chairs from CBER and CDER for being the next panel. Their support and the support of Michelle [00:08:30] Tarver as the center director at the CDRH is absolutely invaluable for the work of the Hub, and we could not do it without their genuine support and commitment. So thank you. I do want to say, and I'm sure you'll emphasize this, please don't read anything into the fact that the two ... The biologic and drug center are the first panel and Dr. Tarver is a separate panel at the end of the day. It is a scheduling problem. It was not originally this way, [00:09:00] but sometimes things happen and this is how it worked out. Thank you, and I look forward to the afternoon.

Discussion: CBER & CDER Hub Co-Chairs

Michael Davis, MD, PhD, Director, Center for Drug Evaluation and Research, FDA
Karim Mikhail, BPharm, MSc, Director, Center for Biologics Evaluation and Research, FDA

Susan C. Winckler: Thanks so much, Amy. And as you noted, it's time to have a conversation with two of our Innovation Hub co-chairs. And so I invite center directors Mikhail and Davis, Davis and Mikhail, to have a conversation. And yes, as noted, we [00:09:30] have a third chair for Dr. Tarver, but she's going to use it later today. She had a scheduling piece, so she will join us later today. Well, we could start talking about something else, but you all made an announcement this week. Should we start there?

Karim Mikhail:

Go ahead.

Dr. Michael Davis:

I think yes. I mean, just timeliness, I think it makes a lot of sense too.

Susan C. Winckler:

Great. Great. So I will say, [00:10:00] when I was looking at it, it looks like the patient voice is a great centerpiece of the initiative. Did I see that correctly?

Dr. Michael Davis:

You did. And that's a very accurate reading of the press release and white paper that we put out a couple days ago for this important announcement. And from the first discussions we've had with Karim and myself and other folks in the center, and [00:10:30] also with external people at meetings that we've attended, we really agreed that you can't really do this type of framework without really looking at how the agency's approaching rare disease review. You can't do it without really putting the patient voice at the center. I think it needs to really inform the work early on and not just be something you sort of look at and almost retrofit at the end because I think it really informs the way the program is constructed and [00:11:00] how the patient voice is incorporated.

And this is something that there's universal alignment with, of the importance of this issue. And I also want to be clear, and I think you could see if you read the white paper that went out with the announcement on Wednesday, that this framework, it's not starting from scratch. Over the past 15 years, there've been a lot of successes within both centers in the agency of incorporating the patient voice, and a lot of really excellent efforts [00:11:30] that have been taking place. We have a patient-focused drug development program and also patient listening sessions. They've made a real difference for how sponsors and the agency gather and act on patient input.

And I can say this firsthand. In my first tour at the FDA, I was in the psychiatry division, and I was working on a rare disease application of a condition that I wasn't familiar with. It was a very rare condition. [00:12:00] We did a patient listening session, spoke with family members, and it made a true difference in how we reviewed the application. I was really just convinced of the importance of doing these. I think we're all aligned that this needs to be more standard part of our work. And also, there's a lot of value of doing this earlier in the program.

The conversations help us understand what symptoms are most difficult, [00:12:30] how the disease affected life, daily life, and what patients hope a treatment will change, what's actually most important to them. And it's also, I think, useful for understanding the heterogeneity of the symptoms that a lot of rare diseases and other conditions, they manifest differently between patients. Even my home turf, clinical psychiatry, a lot of the diagnoses are ... You have five out of nine symptoms where you can have different permutations. And I think that's the case [00:13:00] with a lot of conditions, and really understanding the heterogeneity is very important because I think fundamentally, when you're designing a drug, the goal is to make a meaningful difference to the people who will be taking the treatment. It's just a fundamental question.

And the framework is really giving us a chance to take stock of what we're doing and really think about how we can broaden efforts, take the things that are working really well, [00:13:30] and make this engagement more deliberate. And that's why I think the timing of having this meeting now is very opportune.

In terms of just general comments about the initiative, and Karim will probably have some additional points to add, but the next steps, we're going to be starting up four different internal work streams whose job will be to provide recommendations for changes to internal processes as well as external

communication and engagement because [00:14:00] we want to make this framework a reality, and we also want to do it with, I guess, broad support from agency and center leadership, but really from a bottom-up approach and really taking input seriously for the people doing the work every day, people who are creative and can help us think about a lot of these issues.

Susan C. Winckler:

So let's let Karim jump in because I love the phrase, when you said, "If you're developing [00:14:30] a drug, you want it to matter to the patients." Same for the products that are regulated at the Center for Biologics. So your two cents on ... Okay, you can have five cents on the framework and what this looks like.

Karim Mikhail:

Sure. I mean, let's face it, especially with CBER-regulated drugs with cell and gene, the patient plays a very, very significant role. I mean, if we say that a disease impacts, let's say, a thousand people, [00:15:00] well, those thousand people's voice will really matter. When you're talking about a disease that impacts millions, and if you say that their impact is divided by the number of individuals, you can imagine the weight of the one-person voice when it comes to some of these rare diseases and ultra-rare, specifically when you're dealing with cell and gene therapies.

And because the administration can be different as to where along the continuum of the disease progression, [00:15:30] the risk and the tolerance can really change. So the voice and the perception can be different as to where is the patient in the disease. So it's not a question of just saying, "Oh, let's just hear the patient once in one moment." There is really a continuum across the disease progression. We need to understand the patient perspective at the time when the mutation is identified, later on, once on treatment, and so on. So obviously, this [00:16:00] framework is very critical for us because it will take us a true step forward to transforming the way we review our files. We look very much forward to be working on it with everyone.

Susan C. Winckler:

Yeah. That's so helpful to get a little more color to the white paper, in having the insight from both of you. So let's talk a little bit more about the patient voice dynamic here, and we're going to get this from the staff directly [00:16:30] in your centers in a bit, but would each of you describe how and when the patient voice should be included in the development and review timeline, and how that information is useful to reviewers and others? You just gave us a great example, that a snapshot perhaps is not what we're looking for, but rather the video and more insight. Why don't you go first on this one and then I'll make sure he gets his two and five sentence too?

Karim Mikhail:

I mean, the current practice-

Susan C. Winckler:

Two cents. [00:17:00] All right.

Karim Mikhail:

The current practice is, obviously, we have a lot of voice of the patient at the time of an ad comm. And for example, we've had an ad comm in the last few months. We had two of them back to back where we've had patient participation. And the question really becomes ... Obviously, it is very valuable at that point in time, but is it the most opportune time for us to have that?

Now, what is good is that at the FDA and different teams are doing way more efforts to have earlier patient voice. [00:17:30] As you know, there are early listening sessions, there are dedicated meetings which are incredibly valuable, which are being used. But at the end of the day, currently, I would not consider them as ... Sponsors, at least, don't view them as a necessary part of the process. We view them as incredibly valuable, but the sponsor has to also realize that they're incredibly valuable. So we're trying to make sure that in the future, the framework would make these, honestly, a true [00:18:00] essential part of the process, or else how are we going to be able to review moving forward?

Susan C. Winckler:

And so I hear you say not only a part of the FDA process, but a part of the development process, that you expect sponsors to be contributing.

Karim Mikhail:

Correct.

Susan C. Winckler:

Excellent. Dr. Davis.

Dr. Michael Davis:

Yeah, no, I agree. There's three parties involved, really. I think it's the FDA, the company developing the drug, and I think it's patients and groups of patients to [00:18:30] work together. So in terms of when this input would be useful, I think definitely earlier. And the other aspect of earlier is because it's really setting the program up from the start, a solid foundation for the program I see as very important, rather than going through the program, and then once all the investment into the trials and conduct of the trial is done, then on the back end, looking back and maybe question, "Well, [00:19:00] why did we do certain things in the program?" So I think on the company side, but also the agency side, early is important.

In terms of the other aspect of how ... I think in terms of the specifics, this is something that, I think, going back for the request for information, we'd love to hear from external stakeholders, but also I want to hear from the work streams that we're going to be launching quickly and aggressively, what's most [00:19:30] useful to the reviewers, and from the reviewer's experience working with companies and patient groups, to really get the details right on this. I mean, I have some ideas and hypotheses, but I want to sort of follow the process and make sure we're doing the right thing.

Susan C. Winckler:

And so as we are thinking about the framework initiative and the efforts here, what are some things that you each would like to make sure that folks see [00:20:00] when they're evaluating that announcement? So I guess imagine you have a highlighter. What would you have highlighted in the document that you might want to make sure not only that sponsors saw, but patient groups saw, and other researchers?

Karim Mikhail:

I mean, the first one is the objective of the day. Obviously, it was the number one as the voice of patient. And interestingly, one of the very first meetings we were with also, a group of patient communities, I remember very early on, at least in my acting time, which is great to also [00:20:30] always start with the voice of the patient. But there are other elements that I will highlight also. You'll see there also the voice of experts. And we're dealing with many rare diseases where scientific expertise is not so common. So currently, again, if you look at how we get this scientific expertise, part of it is in an ad comm, but not every product has an ad comm. At times, we reach out, but that's highly unusual when we reach out earlier. Wouldn't it be great in many of [00:21:00] these disease entities where there are two, three, four experts in the world, to actually talk to them early on in the clinical development, make sure that their input is taken into account in what we do?

I will just cover one more, and then I'll leave the other two, Mike, because I know we will be aligned. The third one I want to talk about has to do very much with what is attainable in terms of clinical trial design. And by the way, rare diseases [00:21:30] is not the only area where we have challenges with the practicalities of clinical trial design. I'll mention also, for example ... Vaccines, by the way, is an area where there are other challenges where they have different approaches. So it's not uncommon that we have disease entities where we have challenges with how practical it is to implement a clinical trial program. So we need to think of what is the attainable evidence within what we have, because we're dealing with very, very complex disease entities. We definitely [00:22:00] need to keep the level of scientific rigor and the safety where it needs to be. There's no question there, but we also have to be very practical at what is truly attainable in terms of clinical trial design. Mike?

Dr. Michael Davis:

Yeah. No, I agree with what Karim's been saying. So thinking about the patient voice specifically, I think that what I'd like to really hear from this meeting is just different perspectives on [00:22:30] specifics, in terms of incorporation of the patient voice of what the context ... Is it when an endpoint is being developed, thinking about an outcome measure? Is it regarding selection of a measure? Is it regarding the design of the trial? So kind of specifics on the timing.

And then I also would like ... I think it's useful, because like I said, I think there's been [00:23:00] some excellent efforts that have been going on within the agency, and I'd like to hear a little bit more about what have been the perspectives on the value of it, or feedback. Are there certain aspects of ... Say, for example, is there a program that is particularly valuable, but you think it might be useful if it was at a different time in the program? And things like that to help us really take stock of what we're doing because I think this can help inform [00:23:30] the whole framework initiative, to really make sure, as we're giving a lot of attention across the agency into how we review rare disease applications and how we work with patients and companies, to help support the best types of programs. I think it's a very good time for us to take stock of this important issue.

Susan C. Winckler:

And it strikes me as you both are coming ... You're relatively new in your [00:24:00] positions, and yet now you are official and are thinking through this activity with the Innovation Hub and then the new initiative. Mike, Dr. Davis, you gave us some insights into thinking about that patient voice. What would you add in saying ... What do you most want to hear from today's meeting as you think not only about the framework, but the broader Hub activities and [00:24:30] all it is that CBER's doing thinking in the space of rare disease?

Karim Mikhail:

So it is a real opportunity for us to have this open dialogue and to hear from the patient perspective what they think is important to be incorporated. We are making assumptions as to what we think would be valuable for us. So our mind goes very quickly to clinical and development. We go to where our anchors are, if you see what I mean.

Having said that, I think it's very important [00:25:00] that there is a bit of an opportunity for freedom for the patient groups to express what's important for them. I'm specifically ... Because of gene therapies, specifically interested in the voice of the patients across the continuum, because I have seen at least data that showed that the risk tolerance is very, very different when the patient is diagnosed versus later on. So if that's the case, how [00:25:30] can we use that? What does this mean in terms of clinical trial design? Are we going to focus on a specific administration window or not? How are we going to handle this?

So there are true clinical development questions. Once you get into that level of detail of the patient voice, there are real questions as to how are you going to execute a clinical trial? What will be the timeframes? Would you account for these periods, or would you assume and extrapolate beyond them? I mean, there [00:26:00] are real questions. So I'm keen to listen, and I'll be able to dedicate some time. So I'm happy to be here.

Susan C. Winckler:

Excellent. Because I know the pulls on your time, I imagine you're frequently triple booked. Is it now quadruple booked?

Dr. Michael Davis:

Yeah, that sounds about right. Yeah. I mean, I'm really excited and just really geared up to do the right thing for patients as the ultimate stakeholder here in the work we do, and really just serve the public. [00:26:30] I work very hard, as people can attest, and I've determined I'll work just as hard or harder than anyone else because the work we do is just so important.

Susan C. Winckler:

Yes. Oh, absolutely. And we appreciate you investing the time. I know you both had said you have the opportunity to stay and listen. And if I could, I think what I hear you both said is that ... If I may characterize it, you're saying you not only want to listen, but to have that dialogue, that that's part of

gathering the voice [00:27:00] of the patient, is perhaps there's the follow-up question and the thinking about it in more than just ... Again, not just capturing a snapshot, but thinking through it and having that conversation.

Dr. Michael Davis:

Yeah. And I just really encourage people who will be speaking to just be frank and real, because just even before the meeting started, just hearing from attendees and just hearing their honest thoughts about these issues, I think that's really where the progress can be [00:27:30] made. Just having a frank discussion about this. I think that's very useful for us as we consider.

Susan C. Winckler:

As well as taking the opportunity to respond to the RFI, to the framework, right?

Dr. Michael Davis:

Yeah, and various channels. Yeah, I agree. Good point.

Susan C. Winckler:

Yeah. That there'll be many opportunities. All right.

Karim Mikhail:

And this is just the beginning. I mean, we just launched the framework.

Susan C. Winckler:

And then the rest of today, we'll invest in hearing the patient voice. So appreciate the two of you in [00:28:00] taking the time from your responsibilities, leading all of the center to say you want to invest it in hearing this conversation today about the patient voice in rare disease medical product development. So thank you for joining us.

Dr. Michael Davis:

Yeah. Thank you, Susan, and thank you for everybody for attending today.

Panel Discussion: Grounding in Existing Mechanisms: Where the Patient Voice is Sought Across the Development Timeline

Robyn Bent, MS, RN, Director of Patient-Focused Drug Development Program, CDER, FDA
Cynthia Grossman, PhD, Director, Division of Patient-Centered Development, Office of Innovative Development, Office of Strategic Partnership and Technology Innovation, Center for Devices and Radiological Health (CDRH), FDA
Carmen Matos, MA, Senior Health Scientist, Office of Public Engagement, Office of Public Affairs, Office of the Commissioner, FDA

Susan C. Winckler:

Fabulous. Thank you so much. So as we have center directors Davis and Mikhail step off the stage, I'm going to invite staff from each [00:28:30] of their centers and from CDRH to step onto the stage. So if I could have our panelists step to the stage. So specifically I'm calling up Robyn Bent, Dr. Grossman, and Carmen Matos to come and join our conversation. I was going to move chairs, but it seems just easier if I stay in my seat. There you go.

[00:29:00] So thank you each for joining us and for helping ... We wanted to have this part of the conversation to remind folks, there'll be some folks in our audience who are very familiar with the efforts of FDA to hear the patient voice, particularly in rare disease product development, and then there are many who simply may not be aware of all the opportunities that we have. So we're going [00:29:30] to try to cover all of that in our conversation today.

I will note as we get into the conversation that at the foundation, we had aspired to create an infographic to capture what we were seeing as the opportunities to engage. You see it says, "Hold," because it's not quite done. But what I was struck by is that there were opportunities to engage at the center level and then opportunities [00:30:00] across the agency because the interplay between the centers and then with the office of the commissioner is so important. So that intentionally says, "Hold for infographic," because then it means that I and the rest of the foundation team are really going to get it done and get it posted. And we hope to have it be even interactive. So if you want to say, "Oh, I didn't know about that," can you then get a little bit more detail about it. So stay tuned. And by the way, this means I'll be in your inbox, asking for some additional input [00:30:30] on that.

But let's begin our conversation with the office of the commissioner. So as we see on the slide and then sitting to my left is Carmen Matos. And you serve as a senior health scientist in the Office of Public Engagement where your day-to-day job is facilitating cross-cutting activities. So tell us a bit about the patient voice activities you highlight. What would you highlight about what it is that the office of the commissioner does to facilitate gathering the patient voice?

Carmen Matos: [00:31:00]

Thank you. It's truly wonderful to be here, especially surrounded by people who really care about the rare disease communities. Patients are at the heart of FDA's work. And in the Office of the Commissioner, our role is to be an open door for patients, caregivers, and advocates who want to connect with the agency and make their voices heard.

The FDA regularly engages with patients and caregivers through many ways. As Dr. Davis mentioned, one of the programs are the Patient Listening Sessions, and they provide a direct opportunity for the FDA staff to learn from patients and care partners what matters [00:31:30] most to them, whether it's managing a condition or what they would like to see in a future treatment. These are small non-regulatory meetings, typically about an hour and a half where the patient and care partner and patient community can connect with FDA staff who work on these diseases and review products that may one day help them.

These sessions aren't open to the public, but that is by design to keep them small just so that the patients and caregivers and community can feel comfortable to share what is most important to them with the FDA staff. And those [00:32:00] FDA staff have the opportunity to learn what living with the condition actually looks like, the daily challenges, those treatment burdens, what is a real meaningful improvement to them. And so they're a valuable educational opportunity, especially for those ultra-rare diseases where the FDA staff may not know that their condition even exists. And for those small communities that are just starting up with an organization, reaching out to us early to know that they exist is a way to do that through these listening sessions. And so if a rare disease community [00:32:30] is interested in a listening session, please reach out to us.

As Dr. Mikhail highlighted, there are the FDA advisory committee meetings. And so I wanted to highlight the FDA's Patient Representative Program, which is in the Office of Advisory Committee Oversight and Management, which is also in the Office of the Commissioner. And this program is unique in that the agency onboards patients and caregivers to serve as consultants on FDA public advisory committees and patient representatives are voices and they also are able to sit alongside [00:33:00] FDA scientific staff to share their perspectives on specific medical products and potential approvals and other important issues that are important to the agency.

And so candidates who are interested in the Patient Representative Program are screened for conflicts of interest. And so once they are appointed, they have active voices and can share what it is like to live with a condition, especially with the scientific experts at the table with them. And so for rare diseases, when the patient population [00:33:30] is small and clinical data is limited, having that patient voice in the room is important and essential in the drug development process. And so sharing that experience is important to share because that experience isn't captured through the clinical data.

And then one last thing that I want to highlight is, as Amy Rick mentioned, is that the patient community is encouraged to engage through public dockets. And so as FDA is developing guidance or looking at new policy, we open [00:34:00] dockets to receive written comments and the patient and caregiver's perspective is very valuable in sharing their comments through the dockets to ensure that their voices and their perspectives are heard in a record. And so that when FDA is reviewing the comments in the public record, their perspectives are captured. And as Amy had also mentioned, I wanted to put in another flag for the upcoming meeting on October 28th and with a docket there as a way for the patient community to share their [00:34:30] input on how FDA approaches rare disease drug development.

And so with that, I just wanted to conclude with that patients are a partner in FDA's work and in the Office of the Commissioner, we're here to make sure that the... And we work together across the centers to make sure that the patient community has a seat at the table.

Susan C. Winckler:

Yeah. And so Carmen, I heard you talk about three different things that are great windows of the different opportunities, right? The kind of closed door, which can be a more comfortable environment for the patient community [00:35:00] to share, but they also have the opportunity to reach multiple centers because the product that we may need may be regulated at any one of the centers. And then the support for the representative at the advisory committee is a very, very public opportunity where the patient voice is gathered and heard. And so that's great. And then of course with the dockets, getting that information. So thank you for [00:35:30] that overview.

Now, we didn't really structure it this way, but I'll turn to the centers because we know much of the product-specific activity at FDA occurs at the center level. So to my immediate right is Dr. Cynthia Grossman. Would you chime in from your role as director of the Division of Patient-Centered Development in the Office of Innovative Development in the Office of Strategic Partnership and Technology Innovation at the Center for Devices and Radiological Health? [00:36:00] It's an entire card, Dr. Grossman, I have to say. What would you highlight as CDRH thinks about this?

Dr. Cynthia Grossman:

Yeah, thank you. So at CDRH, we too sort of share this important saying as, "Patients at the heart of all that we do." So patients being at the heart of all that we do isn't really just a tagline, it's sort of the way that we're centrally structured. And so I want to give you a little bit of a flavor for the mental [00:36:30] map of CDRH in terms of patient-centered development and our division, because I think it helps you understand the pathways to engagement. And we share the same pathways across the agency, but there are some specific to CDRH that I'll touch upon.

So the Division of Patient-Centered Development at CDRH really sees, and CDRH as a whole, sees the value of the patient voice in a number of different ways. And I'll [00:37:00] sort of highlight two, which I think come up, especially in rare disease in terms of unmet needs and also thinking about how the patient voice can inform our benefit-risk decisions.

And so the division itself is kind of structured with two complimentary activities, sets of activities. On the one side, we have a group of psychometricians, economists, social scientists who evaluate patient experience data that's submitted to the agency as part [00:37:30] of device submissions. So we serve as consultative reviews to the larger product health technology, they're called OHTs in CDRH, enough acronyms. So the OHTs, we serve as consultative reviewers to those bodies and help them to understand the sort of data that's being submitted on the patient experience side. By that I mean patient-reported outcomes and patient preference information, and I'll talk a little bit more about that.

On the [00:38:00] other side, the other set of complimentary activities that we do is the broader patient engagement activities. And those activities really help us understand the context of the lived experience of patients living with rare diseases or any disease or condition, and their experience with different types of devices. And so for that, we do rely on the same mechanisms that Carmen highlighted in terms of Patient Listening Sessions as well. You'll also hear from my colleague, Tracy Gray, about a particular [00:38:30] case example.

But those two kind of sides of the coin, the patient experience data and then direct interactions with patient communities to hear their lived experience, that kind of combination is really how we think about incorporating the patient voice at CDRH.

I want to highlight a couple of things that are a little unique, the mechanisms by which we engage that are a little unique to CDRH. One is our Patient and Caregiver Connection. And that's a group of patient [00:39:00] organizations that have agreed to provide us with very rapid input from their patient community through surveys when our Office of Health Technologies have a particular type of question. And so that patient and caregiver community, that list of those organizations, you can find them on our website, but that mechanism, that patient and caregiver community and connection is really a way in which we get [00:39:30] that rapid feedback.

Another specific one is... This is more outward-facing, although we want continued engagement on this. We launched a series of patient-facing educational courses and those were really aimed at helping to... It's called our Patient Engagement Program and these educational courses are really helping to take some of our guidances, like our patient [00:40:00] engagement in medical device clinical studies guidance, and really think about how to translate that and help patients to see where they can become engaged as advisors in the work that we do.

And I guess that leads to the final element that I'll highlight, which is our guidance on engagement in medical device clinical studies. And that guidance really does lay out some of the opportunities. I think it was sort of talked about by Dr. Davis [00:40:30] earlier that it's along a trajectory and the earlier, the better. And so that guidance lays out what are some of the opportunity sets as a clinical study is developing for patients to really think about it, but we also see this as a total product life cycle opportunity from the earliest stages of thinking about a device and its conception and its design and its usability, all the way through to how it's operating in the real world and [00:41:00] understanding that context as well. So hopefully that gives you a flavor.

Susan C. Winckler:

Absolutely. And so intriguing on the two, a couple of different dynamics there, but the ability to reach out and ask questions to the patient community where you have the groups who are prepared to respond as well as the expertise that you provide to help reviewers think about looking at the patient experience. So really appreciate that. And in fact, that [00:41:30] guidance was part of what we were trying to put into an infographic, which is harder than you think, but also helpful.

So we've been talking about various mechanisms to connect or engage the FDA team with the patient voice, but even as you just talked about, Dr. Grossman, the agency's work goes far beyond that. And so let me turn the floor over to you, to Robyn Bent, who is director of CDER's Patient-Focused Drug [00:42:00] Development Program because you look at this with an even, I'd say, wider aperture.

Robyn Bent:

I mean, I think Dr. Grossman spoke to specific efforts, but I think she looks at it with a very, very broad perspective as well.

Susan C. Winckler:

Absolutely, yes.

Robyn Bent:

But I think to your point about the graphic, I think as we think about the graphic, it's really challenging because there's a lot of cross-center collaboration. We work so very closely together. And so I think we've just been struggling with how to really [00:42:30] show all of the work that we are doing here within each one of the centers, but also how we collaborate across all of the centers because there is a huge amount of collaboration. And I think CDER leads the Patient-Focused Drug Development meetings. We coordinate them, but obviously we have a huge amount of input from our CBER colleagues, from our CDRH colleagues when it's appropriate from obviously our internal CDER [00:43:00] colleagues, and sometimes the Human Foods Program if that's something that is relevant to a condition and such.

But I think that, and I was really excited to hear Doctors Davis and McHale speak to this a little bit earlier, is that early engagement is so critically important and it's something that FDA can't do alone. We really need industry to engage with patients early because they're the ones who are boots on the ground, doing the work, designing [00:43:30] the protocols, thinking about the clinical trial logistics, coming up with what endpoints they think are important. And all of those things benefit very strongly from input from the patients.

I think when Patient-Focused Drug Development first started, it started as a way to inform benefit-risk assessments. We started with those 24 public meetings, PFTD meetings, started as a way to inform the benefit-risk assessments. But we so quickly learned that, as [00:44:00] was already mentioned, the time to hear from patients is not only at the time that we're reviewing an application. That's not a great time to find out that the endpoints being measured aren't the endpoints that are meaningful to patients. It's too late to do much. So the earlier we can engage, the earlier Patient-Focused Drug Development meetings can happen, Patient Listening Sessions can happen, the earlier industry engages with patients maybe before they even have a product in the pipeline, but they're thinking [00:44:30] about it, they're thinking about targets for therapy are really... It's really, really helpful.

And I would say I'm not going to go through... I think a graphic will be good because I'm not going to go through a list of all of the different engagement opportunities that we have in CDER. We have a lot and I think there's even more places where the patient perspective is incorporated. I feel like when I'm thinking about our complex innovative designs, when I'm thinking about our [00:45:00] model-informed drug development, all of those are being done with the goal of advancing drug development so that we can get safe and effective medicines to patients faster.

And so I would say we have so many different programs that maybe don't have patient in their name, but they have patients in their heart. And I think that that is a really key, key kind of thing for people to understand, that just because it's not on the Patient-Focused Drug Development page or the Accelerating Rare Cures page doesn't mean that it's not very [00:45:30] focused on what matters to the patients.

Susan C. Winckler:

And what great phrasing to be thinking about this, it may not have patient voice in the title, but it is in the heart of the work that is being done. We may hear... I'm going to guess that people might repeat that later in the day, Robyn, that you'll get credit for the phrasing.

So it's very helpful to ground us in that activity and thinking about what are those formal mechanisms? Let's turn to talk a little bit [00:46:00] about the impact. Might I ask each of you to reflect and share an

anecdote, and it can be as much or as little detail as you're comfortable, but share an anecdote where you saw or heard the voice of the patient and it resonated with yourself and with those working in medical product development for rare disease.

Do you want to go first, Dr. Grossman?

Dr. Cynthia Grossman:

Sure. I don't want to be a spoiler alert for Tracy Gray's [00:46:30] excellent case example in a minute, but I will give a nod to our annual Patient Engagement Town Hall that we hold at CDRH. That's one that goes across CDRH. So it doesn't matter what role you have in CDRH, you are invited to this annual town hall. And it usually covers broad topics about... It can be a particular element of a disease or condition. [00:47:00] Neurodevelopmental disorders was one, for example, and the role there. Tracy will talk about another one.

But what I really want to highlight there is what's the impact of that? The impact of that on the staff is that everybody, first of all, says to us, "Thank you for doing that." It helps us keep who we're serving top of mind. And the fact that it's carved out, that it's planned for, that it's [00:47:30] annual, that Dr. Tarver opens or closes it, makes the time to make sure that it happens center-wide is an endorsement of the import that we see. But also, I think it really, from what we've heard from the staff, it really supports their work. It buoys them. And I think the work that we do is hard and to be buoyed around what the true north of our work is is really important. So I'd highlight that.

[00:48:00] The other one that I would highlight, which isn't necessarily specific to rare disease, but it's a methodology that we know has been useful across diseases and conditions, and that is patient preference. And patient preference methods, we have a guidance out, it went final. And there's opportunities there in that final guidance. We really talk about the suite across the total product life cycle, not just for benefit-risk. As Robyn said, we started there, but then [00:48:30] we've really thought about what are the implications across benefit-risk? And we have some case examples on our website.

One of the case examples I want to point you to is a company that did a patient preference study around transitioning to home solo hemodialysis. So home hemodialysis at home, often supported by a care partner. This company did a patient preference study to show that a subset of patients, not all patients, but a subset of patients were willing to accept the risks [00:49:00] of solo hemodialysis and be open to that. And at that, in fact, there was some safety data that suggested that that influenced the benefit-risk decision-making on our side, and then that allowed for an extended label indication for solo home hemodialysis.

And why is that important? Well, we're excited because the methodology seemed to be useful, so that's always helpful, but also, it's a real patient empowerment story. It's a story about identifying a subset of patients [00:49:30] where they were able to communicate their thinking around the benefit and risk, and then they felt empowered to say, "I can do this myself" for those particular subset of patients. And in a situation where caregivers are sort of implicated, what kind of change might that happen? You can kind of imagine, this is beyond the data, but you can kind of imagine what kind of change that might happen in the home and create for those care partners and for those patients.

Susan C. Winckler: [00:50:00]

So two great examples, both the... I'm struck in your first one about how energizing that then is for the staff, thinking about, you actually gave me more than two, but in the examples, thinking about the patient engagement day, that that's such a... I hadn't thought about it from that perspective about how energizing for the team could be because rather than the computer engagement, it's the individual and thinking about that patient, and then certainly gathering [00:50:30] the patient preference, which then opens the door to those greater opportunities. Thank you.

Robyn, do you want to provide an example? And it could be CDER, CBER, thinking about your experience at the agency.

Robyn Bent:

Yeah, no, I would love to. And I think one thing that I didn't mention in my last response was our Patient-Focused Drug Development Guidance Series, which really it's four different guidances and it starts with engaging patients. It moves on to asking questions in a [00:51:00] way that is accessible to patients, but also non-biasing. It moves then to developing clinical outcome assessments or selecting or modifying clinical outcome assessments, and then finally to using clinical outcome assessments as endpoints for medical product development.

And so I think just as an example, we recently put out our report on how FDA uses patient experience data in regulatory decision-making, and we're seeing that about 73% of [00:51:30] reviews of new molecular entities and about 60% of non-NMEs, those reviews are discussing patient experience data in some sort. Many times clinical outcome assessments, that scientific way to really capture the patient's perspective and their experience with the medical product. And for rare diseases, over 90% of the new molecular entities that have the orphan product designation contain a reference [00:52:00] to patient experience data.

But what I want to talk about really, really quickly, because I know we'll have really great case studies, so what I want to talk about is something that I've noticed just as an internal FDA culture or CDER culture change. And I mentioned this at one other meeting, but I haven't talked about it a lot because I think... But it's been really impressive to me because I've been here for about seven or eight years now.

And so as you all know, we have [00:52:30] a Medical Policy and Program Review Council, MPPRC, where senior leaders will talk about applications or policy implications and things like that. And what I've noticed over time is that more and more often, almost every meeting that we've been to recently, somebody in the room as their discussion is happening will raise their hand and ask the question, "Do we know what the patient perspective on this is? Do we have information about the patient [00:53:00] perspective?" And to me, and it's never the same person. It's not like we're sitting in a room and there's one person's job to raise their hand and say, "But what about the patient?" Right?

Susan C. Winckler:

That's their agenda. I know.

Robyn Bent:

Exactly. It's not that. And so it really is a different person every single time. And to hear them just somebody ask that question and people to have an answer from either a Patient-Focused Drug Development meeting or qualitative research or a Patient Listening Session, and just to really be able to [00:53:30] share some of that. Obviously, it's a starting point, not an ending point, but to hear that and to see how frequently that's happening now is really, really motivating.

Susan C. Winckler:

Absolutely. And motivating on the flip side, right? So you're observing that the question is being asked and then there is the answer that there's the opportunity to point and say, "Well, here's what we have and here's how we considered it." And then to have that as part of the conversation, really helpful.

Carmen, [00:54:00] is there an anecdote or something that you would want to share where you can say, "Oh, when I think back on that, that was such a powerful story or impactful"?

Carmen Matos:

Yeah. So something that we've seen a lot with listening session, and I think this relates a lot to patients being involved early in the development process and clinical trial design, is the impact on families and care partners. It's not just the patient that's living with the condition, but their families as well. Parents, and especially [00:54:30] for pediatric rare diseases, the parents have to change their entire lives to take care of their child or loved one, and then it's also their siblings who are also impacted with their experiences and quality of life. And so a lot of their needs have to be put aside while they're supporting their loved one.

And so that impact is really important in clinical trial design because it also relates to their ability to participate in clinical trials. Traveling to a clinical trial site at a medical center [00:55:00] can be incredibly difficult if they're managing patients with complex care needs, like needing medications that need to be refrigerated or traveling with heavy medical equipment. Those logistical challenges are something to consider and create barriers for them to participate in clinical trials. So understanding those barriers is essential to make sure that the clinical trials are accessible to these rare disease families and something for FDA staff to also consider as they're looking at clinical [00:55:30] trial protocols.

Susan C. Winckler:

And that's helpful too in helping us understand the picture, not only of what the individual patient is experiencing, but that patient's family and the caregiver and their ecosystem around them. I can imagine now maybe even looking a little bit differently as any of us go through the airport to think, "Oh, I want..." What must that be like if you're in a clinical trial with some sort of dynamic that you have to... It might be a device that's [00:56:00] going through review and trying to think through how to navigate that in a daily life. Of course, far more challenging than that, but thinking about the family and the caregiver dynamic. Thank you, Carmen.

So we have just a couple of minutes before we turn to our case studies, which will paint us a picture. Would you each share, we have time for another quick response, share what you hope [00:56:30] our attendees gather from today's meeting? So all the folks who are here in the room or who are listening,

what do you hope that they gather from today's meeting? And Robyn, you haven't gone first yet, so you get to go first for this one.

Robyn Bent:

Great. Thank you. I think that what I hope comes out of this meeting and out of the case studies and it's already starting to come out of the discussions that we heard from our leadership earlier, was that the patient [00:57:00] voice is important early and throughout. In that report that I mentioned, another thing that we noted, our reviewers talked about how important that patient experience data was throughout medical product development. It's not always mentioned at the time of the review because the discussions were held when we were talking about endpoints or talking about clinical trial designs and things like that. But I think that it's really, you'll hear, I think in the case studies and you see in the report that the patient voice [00:57:30] is really important throughout and it's not a air drop-in, hear from the patients once, and you're done. It really is throughout and we need our industry colleagues to work with us to ensure that that patient voice is incorporated throughout. Thank you.

Susan C. Winckler:

So a little bit of maybe what we heard earlier and thinking about the video versus a snapshot and continuing to hear that voice throughout?

Robyn Bent:

Yes.

Susan C. Winckler:

Carmen?

Carmen Matos: [00:58:00]

So I hope everyone here today leaves with knowing that FDA is here for you and there are ways for your voices to be heard. Listening Sessions, PFTD meetings, Advisory Committee meetings, Patient Rep Program dockets, town halls. They're not just programs and formalities, but they're ways for us to work together to support the communities that we serve. And for the rare and ultra-rare communities, we want to hear from you. You're the experts and you really know [00:58:30] your community best. And so if there are any programs and initiatives that you're interested in, you can please reach out to us. If you don't know where to go, you can reach out to our forpatients@fda.gov email and we are here for you and we look forward to working with you and connecting with you.

Susan C. Winckler:

Yes. Repeat that email address.

Carmen Matos:

Oh, forpatients@fda.gov.

Susan C. Winckler:

All right. The number four?

Dr. Cynthia Grossman:

F-O-R.

Carmen Matos:

F-O-R.

Susan C. Winckler:

F-O-R?

Carmen Matos:

Yeah.

Susan C. Winckler:

Good clarification. All right. So forpatients@ [00:59:00] fda.gov. Cyndi, last word here?

Dr. Cynthia Grossman:

Yeah. I would say that I hope everyone takes away that even though we have these different product centers that we're really aligned and that we're communicating, that we're collaborating internally, and that we're really, as you heard from our leadership, and I'm sure you'll hear throughout the day, we want to collaborate with all of you and we want to hear from all of you. And so I think sometimes it can seem like we've got a lot of different [00:59:30] pathways, but those pathways are different pathways for a reason, but there is a kind of coordinated, behind the scenes, coordinated effort across the centers and across the agency to really work together on this. And that also to pick up on what Robyn said, it's both across the development spectrum, but it's also across time. And so we're in it for the long haul.

Susan C. Winckler:

Excellent. [01:00:00] Thank you so much. Please join me in thanking our FDA representatives for joining us today. Really helpful, and yes, we can step off the stage because we're going to use the podium for the next session, but helpful to be thinking about and understanding those formal mechanisms that FDA has to gather the patient voices rather, as well as to stimulate the gathering of that patient voice.

Case Studies Presentations

Terry Pirovolakis, Founder & CEO, Elpida Therapeutics/CureSPG50
Tracy Gray, MBA, MS, RN, Health Scientist, Patient Engagement Lead, Office of Innovative Development, Office of Strategic Partnership and Technology Innovation, CDRH, FDA
Emily Machiela-Leestma, PhD, Coordinator, HD Benefit-Risk Initiative

Susan C. Winckler:

So the next segment of our [01:00:30] meeting today is to think about and hear from specific case studies. So we have three different case studies that will be presented, and we're just going to jump into the first one. So I'm going to invite CEO Pirovolakis, who you founded and you are the CEO of Elpida Therapeutics. So welcome to the stage. We're so glad to have you, and the clicker is right [01:01:00] there.

Terry Pirovolakis:

Amazing.

Susan C. Winckler:

You control it.

Terry Pirovolakis:

Thank you so much. Can everybody hear me okay? Awesome. I just want to say it's unbelievable that I was here seven years ago in that back room, a lost father trying to save his child. So I want to thank the Reagan-Udall Foundation for including me today and allowing me to present my journey.

So my name is Terry Pirovolakis. This is my amazing son, Michael. He was born on December 17, 2017. [01:01:30] And after an 18-month diagnostic odyssey, he was diagnosed with something called SPG50. We were told, "Go home and love him. He'll be paralyzed from the waist down by the age of 10. He'll be quadriplegic by the age of 20. He'll never walk, he'll never talk. And there's nothing you can do about it." We lost our minds as parents and we decided that we had to do something, no matter what it took, to help this little boy.

And a month after diagnosis, I met Dr. Steven Gray and Dr. Xin Chen at UTSW who [01:02:00] we decided to work together and make a treatment for Michael and the other children affected by this devastating disorder. Two weeks after that, we came to our community and we said, "We need your help. We have to raise $4 million and we have no idea what we're doing." They made a beer for Michael. They did a Beer Works for Us. We raised $25,000 and that kicked off the journey, which we call the Journey to Cure Michael, and allowed us to have this confidence that we could actually achieve this incredibly impossible goal of making a therapy and raising [01:02:30] 4 million. And I'm just going to put together this... I'm just going to show this video very quickly that just talks about our family, the story, and puts everything together.

Georgia Pirovolakis:

Hi, baby.

Terry Pirovolakis:

We're going to cure him. That's what we're going to do. We're going to cure him.

Georgia Pirovolakis:

Or give him the best shot.

Speaker:

Look at all that stuff to play with. I guess I should have recorded that. So tell me, what's Michael like?

Georgia Pirovolakis:

He's a pretty happy kid in general.

[01:03:00] Michael is a happy little guy. He works really hard to do basic things that other kids do naturally, but he never gives up. He keeps going and he tries with all his will to do simple tasks like crawling, [01:03:30] and walking, and feeding himself, things that we all take for granted.

Initially it was hard, and it's still hard. Every day is a little harder because Michael has now started to not reach the milestones he should be reaching. He's not walking, [01:04:00] he's not talking. And so, that affects you internally as a family.

Terry Pirovolakis:

There is nothing. There's no drug. There's no treatment for Michael's specific disease.

Georgia Pirovolakis:

When we [01:04:30] were told about Michael's diagnosis, they just said, "Go home and just live your life, but don't expect much from your son. He will be in a wheelchair. He will be nonverbal. He will be delayed, and there's nothing we could do for you."

Terry Pirovolakis:

Doing nothing is impossible. We can't just sit back and say Michael can fall apart and that's okay. That's not okay for us. We'll do everything possible for him.

Berge Minassian:

There's a process [01:05:00] that could help Michael, but it involves this very expensive approach. [01:05:30] Alzheimer's disease, multiple sclerosis, Parkinson's disease, ALS, and I can go on and on, all of these common diseases are genetic diseases that are more complex, meaning more than one gene is involved. To fix those diseases, we need to learn first how to fix the diseases where single genes are

defective, such as Michael's disease. It is the research in these rare, terrible diseases of children that is going to be the springboard for us [01:06:00] to figure out how to treat the common diseases that afflict every one of us.

Georgia Pirovolakis: His prognosis is his future looks bleak. He can't fight for himself, but that's why we're fighting to do it fast and quick. So we're just hopeful. We're hopeful that we make it. It's hard.

Terry Pirovolak...: Hey. Hi.

So then [01:06:30] we started doing galas, and golf tournaments, and lemonade stands, and everything you can humanly imagine. And we were fortunate enough to raise four and a half million dollars over three years to allow us to do the therapy and the... Thank you very much. To allow us to do the things that we need to do and make sure that we weren't pausing. [01:07:00] And then as you can see, Michael was making gains. He was almost walking at one point. At the same time, the therapy kicked in and after a three-hour seizure, which almost took his life, he actually went backwards in his progression.

And then Dr. Gray and Dr. Chen came back and showed that we're able to restore function in the animals where a normal animal will do well to spread eagle, where an affected animal will do hind limb clasping, and be able to restore that function. And then thanks to the collaborations [01:07:30] and the companies you see on the screen, we were able to get Health Canada approval on December 30th of 2021, and Michael was treated at SickKids in Toronto in March of 2022, thanks to the amazing support of thousands of people around the world.

And then we decided that we had to do more. We had to get more children treated. In August of 2022, we got approval from the FDA. Thank you, FDA, for supporting us. And we treated two more children, and it took a village. It took a community and a village, and hundreds of people from around the world to make [01:08:00] this happen. We then decided that we had to do more, that more children deserved a better life. So we formed Elpida Therapeutics, a nonprofit 501(c)(3) formed from Columbus Children's Foundation from Sheila McHale, Fundacion Columbus from Javier Garcia, and my wife and I's foundation, Cure SPG50.

We since treated a bunch of children for SPG50 in regards to this conversation here. My family's foundation was the PAG or the [01:08:30] patient advocacy group that aligned with Cure SPG50. For CLN7, we're working together with a small foundation that's unfortunately because it's such a quickly fatal disorder, there isn't a PAG that's come together, so we're bringing one together. For CMT4J, we work with Cure CMT4J and for Chelsea's Hope. For the four, we're working with Chelsea's Hope as well.

It couldn't have been done possible without the partners and the companies you see on the screen. Today, we've treated [01:09:00] 18 children across three different disorders. SPG50, we treated 16, CLN7, one, CMT4J, and by the end of the year we'll have treated 48 children across all these disorders. We have seven countries and five different clinical trials up and running. I want to thank the FDA for all the guidance that you guys have done over the last two years or longer that have allowed programs to come into the clinic. The guidances that you guys have provided us have allowed us to move very, very quickly, [01:09:30] not just in my program, but many more. And as you can see, there's a lot of roadblocks along the way, but the last one that we don't need is the FDA to be there, and you guys have been there supporting us through this journey.

The problem that we have now is we need support, and the guidance unfortunately was out before this presentation was created, is how do we get a drug to approval on these rare conditions? My son's disorder has a hundred children in the world. CMT4J has 23, CLN7 has 45. How do [01:10:00] we get those programs to approval without doing $50 million in five years of CMC work?

The lessons learned that we have here is patient voice needs to be there from day one. We need to make sure that they're included in the regulatory discussions, the trial design along the way. Embedded in our teams is a patient organization representative.

Set realistic therapy expectations. When Michael was treated, there was only SMA. We thought Michael would be walking [01:10:30] and talking and living a normal life. That's far from what we are seeing. We're seeing Michael is leading a better life and these children are leading better lives, but they're not cured. I think that's something that we need to set the expectation at, because otherwise the [inaudible 01:10:45] scales and all the patient advocacy scales are all going to be thrown off because we're all expecting something drastically different than what we're seeing.

Getting natural history right. As patient organizations, we're told to fund natural history studies. We do retrospective, we do chart reviews, [01:11:00] and unfortunately those are not good enough for standards at the FDA. They're way off. I think what we need to do is realize that that's what we have, this is what we are producing, and trying to find a way to blend that together and find key elements that work within there. I think the guidance that was provided yesterday is trying to get us there.

Choosing meaningful endpoints. The FDA has been extremely supportive through all of our programs to help us get it right. Unfortunately, I think a lot of the times [01:11:30] all of us have misunderstandings around what endpoints are needed. I think we need to work together to say we thought this one would work, we thought this one would work, we're getting close when we're not fully there. And not go back and do another study, but maybe understand are we seeing the inclination of efficacy to help us get to the end?

And just like Dr. Mikhail said and Dr. Davis said, we need to listen over time, right? This is not a point in time. We're doing a phase one, we may do a phase two, we may do a phase three. [01:12:00] Hopefully we don't have to do those, but it's a listening and it's an understanding throughout this period of time, and never stop advocating.

The last one is a plea that I put up after every single presentation I do going forward, and it's a plea that thankfully the FDA is listening to us, and it's that we need to find a path now to help these families move quickly, and you guys are understanding that and supporting us. I'll tell you a story, because the plea is now old. I had a call yesterday at the airport [01:12:30] from a father that had CLN7, and our trial is enrolled. It's done and there's no more room for these children. These children are going to die within four years. This father was showing me he had his passports ready, he's been raising funds, he's willing to do anything humanly possible. He messages me every other week, and I had to tell him that we unfortunately let him down. We didn't make enough drug in the trial to treat his child, and it's going to take us between five and 10 years now to make the product in the fashion that meets the requirements [01:13:00] of the FDA today.

I think that if we can work together, families will not have to bury their children, that we will find a way together so that the children that are existing today also have an opportunity, not just the ones in the

future. I just want to thank the FDA and everybody here, and all the staff for supporting us and being there for us. Thank you.

Susan C. Winckler:

Thank you so much, Terry, for sharing your experience [01:13:30] with us so that we can learn, and particularly those lessons learned that you teed up.

All right. We'll turn the podium over now to hear a case study from FDA itself. I will turn the podium over to Tracy Gray, health scientist and patient engagement lead in the Office of Innovative Development within CDRH. Scientist Gray, it's your time.

Dr. Tracy Gray:

Good afternoon. I just have to say what an amazing real life example of what can be done and [01:14:00] congratulations to you for all that you've done for your son and on behalf of other patients.

You've heard repeatedly how patients are at the heart of all we do and it's truly true. I have the privilege of working with Dr. Cynthia Grossman on her team to lead patient engagement efforts within CDRH. And today, I chose a use case example that will demonstrate the perspectives of patients and caregivers from the rare disease [01:14:30] community and how they've helped FDA to better understand their experiences using devices outside of a professional healthcare setting, and considering to how FDA can make sure that they're safe and effective for use in that home setting. Because everybody would rather be at home to the extent possible, and have the kind of life that they'd like outside of a healthcare facility, particularly when you're talking about rare conditions where you're often... [01:15:00] Have experience going back and forth for care.

You also heard a little bit about how we have an agreement with some organizations so that our staff can get timely feedback and hear from patients on various regulatory issues, and so these are some of the organizations listed on this slide. We have 26 current partners that demonstrate the organizations, those agreements that are in place and [01:15:30] they're available for our review teams to interact with when they have a regulatory question. They give us timely feedback that really helps in making our decisions, and we leverage our relationships with these organizations as well as other patient organizations that we meet that can really help to bring us insights that are important for our staff to hear.

Now I'd like [01:16:00] to give you some context before sharing the use case example of patient insights on home use devices that were shared by the rare disease community in one of our CDRH town halls, which is an internal event. The town halls allow us to hear from staff, to hear directly from the patient community or their care partners on topics that are related to medical device regulatory work. Recently, our director, Dr. Michelle Tarver, stated [01:16:30] that nearly 50 million Americans were already using some form of a remote patient monitoring device as of 2022, and that the US home medical equipment market is projected to nearly double by 2034 as more Americans are managing their healthcare with devices in the home setting.

To make sure we're on the same page, I just want to clarify some terms that you'll hear me use. A home use device is a medical device [01:17:00] that's labeled for use in any environment outside of a

professional healthcare facility. That's how we refer to it. And that could be at home, it could be an outdoor environment, an office environment, schools, it could be in the car, it could be in an independent living facility. But when we refer to a user, it's anyone who directly uses the device that provides assistance or provides assistance in using the device, so it could be the patient or [01:17:30] a care partner.

As noted on this page, the growth of home healthcare has resulted in more frequent use of devices in the home setting. Home use devices are becoming more common and they're also more complex. You heard the mention about home dialysis in the home setting. FDA wants to ensure that these home use devices are safe [01:18:00] and effective.

With these considerations in mind, I selected the use case example of a CDRH town hall that was conducted in September of 2023. The objective of the town hall was to hear the perspectives of the rare disease community on home use devices, including the importance of home use devices, human factors, usability designs, the importance [01:18:30] of instructional information, and support mechanisms in the home setting. We worked in collaboration with the National Organization for Rare Disorders to identify and recruit a panel of about eight patients and their care partners who shared their insights on an FDA moderated panel discussion.

This slide represents the range of device experiences that were shared by the panelists during the town hall, and you'll see that includes [01:19:00] respiratory, neurological and mobility, gastrointestinal, and diagnostic devices.

This slide reflects what our panelists felt was important to them when considering devices used in a non-traditional setting. This included access to home use devices that allow patients more flexibility and the ability to participate in more activities, resulting in a greater quality of life compared [01:19:30] to a clinical setting which is much more restrictive. Even though they appreciate the flexibility offered by using devices in a non-traditional setting, they felt there does need to be some improvement in the functionality of the device to better accommodate one's lifestyle in their daily life.

In addition, there are opportunities to address challenges related to health equity impacting racial and ethnic minority groups and individuals who have cognitive impairment, as well as those who lack [01:20:00] speech or fine motor control. They noted that getting information, instructions and support of a device for a progressive condition is difficult. Even if you received initial instructions for how to use a device, your informational needs change over time because of the progression of the condition. However, they also expressed a concern about the lack of support and preparation for transitioning from a device in a facility to [01:20:30] a non-traditional setting. Oftentimes, you have more healthcare givers or professionals in the healthcare setting than you would in your home setting. They talked about the need to have more support. They noted that there's an information deficit when we're talking about off-use label of devices, which is common for the rare disease community. They felt that clinicians often don't have this information and it's beneficial for them to have access to be informed.

[01:21:00] The input that we received during the town hall helped us to understand the device needs of patients, and considerations that may allow them to spend less time receiving care in a traditional setting and more flexibility to participate in activities that will allow them to have a better quality of life. However, further consideration is needed to ensure that patients with rare conditions are equipped to safely and effectively use devices outside [01:21:30] of a healthcare facility.

Thank you. This use case example about considerations for home use is expressed by members of the rare disease community, and it's relevant to two of the CDRH initiatives that you'll hear about later today from Dr. Michelle Tarver, and one those initiatives is home as a healthcare hub, and the other is the Rare Disease Initiative. Thank you so much for your time and attention.

Susan C. Winckler: [01:22:00]

Thanks so much, Tracy. Very helpful, that's okay, to think about how then CDRH used that example to go specifically partner with the rare disease community. Our final case study, come on up. Actually, you don't need the clicker, do you?

Emily Machiela-Leestma

I do not.

Susan C. Winckler:

All right, but you do need the microphone.

Emily Machiela-Leestma:

I do.

Susan C. Winckler:

We will turn now to Emily Machiela-Leestma, who is coordinator of the HD Benefit Risk Initiative. [01:22:30] Thank you for joining us, and take it away.

Emily Machiela-Leestma:

Thanks. Thanks for the introduction, and thanks to Reagan Udall for giving me the opportunity to speak on behalf of the Huntington's Disease community today. First of all, congratulations. You're one of the few people that get my name right on the first try, so thanks. I do not have cool slides, and there's a specific reason why. I understand that this is a panel on case studies lessons learned, and the HD Benefit Risk Initiative is new. We're still in the launch phase. [01:23:00] However, the organizations that are part of the HD Benefit Risk Initiative are not new. They're advocacy organizations that have worked in Huntington's Disease for many, many years. And so, I'm going to speak a little bit today on some of the lessons we've learned over the years in advocacy work in HD, and also what we're learning and coming together to help get the patient voice incorporated into decision making.

To give you a little background on Huntington's Disease, Huntington's Disease is an autosomal dominant neurodegenerative disease that affects [01:23:30] movement, cognition, there's also psychiatric symptoms. Because of the autosomal dominant nature of the disease, it affects families holistically. Children that have parents that are affected by HD have a 50% chance of inheriting the disease themselves. They become caregivers at a young age to their parents, and they watch their parents or family members slowly lose independence over time. HD is a slowly progressing disorder, [01:24:00] so

these things happen over decades and they slowly lose independence. There's currently no disease modifying therapies for HD.

The HD Benefit Risk Initiative is just a fancy term for all of the patient advocacy organizations in Huntington's Disease to come together to better incorporate the patient voice in Huntington's Disease regulatory decision making and clinical trial decision making. The HD Benefit Risk Initiative grew out of conversations, first of all, between our community and advocacy [01:24:30] partners. We've had these conversations, especially over the last year, amongst each other and amongst the community on how we can better incorporate the patient voice. And then it also came about through the FDA, and I want to talk about this specific case study and how the FDA has helped challenge us to come together as a community to better represent the community holistically.

The FDA convened a round table for all Huntington's Disease advocacy partners and associated clinical [01:25:00] and research partners to talk about some of the challenges. And what we discussed centered around one difficult question, and that is how do people living with and at risk for HD weigh the benefits and risks of new treatments? After that round table, all of the HD patient advocacy organizations, together with research and clinical partners, agreed to try to answer that question together. Typically, this is done by industry partners, benefit risk is tied to product specific developments, and [01:25:30] what we're looking to do is to create a better holistic view of the patient voice from advocacy partners to incorporate that earlier in development.

Like I said, the initiative is pre-competitive. It's not tied to any product, sponsor, or program, and our goal is just to understand as completely and honestly as we can, how people across the HD community think about benefit and risk, and to share what we learn with the community and with everyone that makes decisions that affect the community. We haven't decided in advance what any [01:26:00] answer looks like. We're just trying to see the community exactly how it is. It sounds really nice in theory, but it turns out to be much more difficult.

The story that we just heard from Terry, which is such an important story, and I'm honored to be on a panel with Terry, his story has inspired me for quite some time, is moving mountains for one child. In HD, things are a little bit different because we're on the other end of the spectrum. We're rare, but we're not ultra-rare. Tens of thousands of Americans are living with symptoms of HD and many more are at risk, [01:26:30] and the disease is slowly progressing, so people are living for decades and slowly losing their function. The story in HD and the patient voice in HD is not just one patient voice. It's very heterogeneous and it changes over time, as we've heard about today.

The reason why I say the patient voice is not just one patient is because when we talk about patient preferences in HD, we're really talking about many different people at many different points in a very long story, [01:27:00] sometimes over generations. For example, you have a 20-year-old that has decided to get tested early and finds out that they have the gene that causes Huntington's Disease. They may live decades without symptoms, but they carry on in life knowing that knowledge. You have someone in their 40s who doesn't show symptoms and remains untested, and that's okay, and their voice is important too. You have someone maybe in their 50s or 60s that is beginning to show symptoms and making decisions about their life. And then you have a parent [01:27:30] that has a child, is caring for a child that has a particularly devastating form of Huntington's Disease called juvenile Huntington's Disease. All of these perspectives are important to incorporate in the patient voice.

The real challenge is, how do you incorporate very heterogeneous life experiences at different points in time into decision making? It's a question that's difficult to answer, and I think the reason why we're all here today. What we've found over years is that in [01:28:00] Huntington's Disease specifically, there's four things that really shape what the patients are answering when it comes to benefit risk and patient preference information.

The first is knowing. Because we are a monogenic autosomal dominant disease, you can know, like I said, decades before symptoms occur. Knowing or deciding not to know surely affects decision making one way or the other.

The second is time. HD unfolds over decades and what people [01:28:30] weigh likely changes as the disease progresses, like we've heard about earlier today. We're not looking at one snapshot, things that are important earlier in disease become overtaken by other priorities later in disease, and we need to represent all of that holistically in patient preference information.

The third is uncertainty, and it's something that I want to touch on a little bit because I think it's specific to HD, but can be really used as a model for other rare diseases as well, because I know this [01:29:00] happens in other diseases, and that's uncertainty. People that are from HD families carry a lot of uncertainty. I'm from an HD family myself, and so I know this firsthand. The first bit of uncertainty is if, right? If we will develop the disease. The second bit of uncertainty is when. The CAG repeat expansion that causes Huntington's Disease, the length of that repeat tells you a lot about the age of onset, but it doesn't [01:29:30] tell you everything. People with identical or similar CAG repeat sizes can show onset of symptoms decades apart.

The third is how it will show up. HD is very heterogeneous. Some people have movement symptoms that are very forward. Some people present with more psychiatric symptoms, and the weight of uncertainty in families for if, when, and how, is heavy. And how do we incorporate that into decision making? It's really, really important. [01:30:00] I'm not saying that patients are unwilling to carry more uncertainty with treatments. I'm just saying it definitely shapes decision making.

The fourth and last thing is just the full spectrum of disease. Like I said, there is a particularly devastating form of the disease called juvenile Huntington's Disease, and then there are people that are learning about HD in their families for the first time with someone being diagnosed in their 70s or 80s. All of these different perspectives certainly have a little bit [01:30:30] different answer when it comes to what risks are you willing to take for what benefit? And so again, the challenge is how do you incorporate all of that into one holistic voice? The most honest answer is probably that it depends. I think that, it depends, is actually really important information if we frame it correctly.

That's where I think HD is a model, a model for how to incorporate the patient voice early in any sort of decision making [01:31:00] agnostic of any product. The complexity can sound like a reason why this is too hard or too messy for regulatory science, but I'd argue it's the opposite.

Because of some of the unfortunate features of Huntington's Disease, I think it can be an opportunity to be a model for how to incorporate the patient voice better, like I said, earlier in disease. HD is rare, but not ultra-rare. You have tens of thousands of people living with symptoms, so we have a relatively large population as it goes for rare disease, [01:31:30] and so we can maybe better stratify throughout time points in disease course how these preferences change. It's also caused by a single gene and it's

autosomal dominant, so like I said, it devastates families. Many people that are affected by Huntington's Disease have also watched their parents, or grandparents, or aunts, or uncle be devastated by the disease. Because of that, these patients are informed.

I don't say that every patient is informed. Of course, this is always a spectrum, [01:32:00] and some people are learning for the first time. Some people choose not to know at all, and their voices are still important to be heard, but a lot of these patients and families are informed because it's been part of their daily lives for so many years. I think that gives us a unique opportunity to really engage people in these kinds of benefit risk initiatives and patient preference information.

Why does any of this matter? This matters because we know, everyone in this room knows that every choice made [01:32:30] in developing new treatment rests on assumptions about the people it's for, who should be in a trial and at what stage, what a trial should measure, how much we should ask people to give in time, in procedures, in travel? These are all really important considerations for clinical trial design. And in the end, whether the benefit is worth the risk. In HD, every one of these choices looks different depending on who you ask. A person with no symptoms and a person 10 years into the disease may weigh the same [01:33:00] treatment very differently. If we only hear from one of them, we end up making decisions for the other. And I want to be clear about one thing. Preference data we know informs a decision, it doesn't make it. But what we're trying to do with the HD Benefit Risk Initiative is to make sure that the people making that decision are looking at the whole community and not just the ones that are easiest to hear.

So a few lessons that we've learned so far and things that we continue to learn right now on a daily basis. And the first lesson is [01:33:30] the simplest, that no single organization can answer this question alone. We all represent different parts of the community, some young people, some families, some researchers and clinicians. And the questions the FDA is asking, and frankly all the advocacy partners are asking, we need all perspectives incorporated. The second lesson is that the data that we already have are built for different purposes. So many advocacy organizations that I work with [01:34:00] have worked for years to help understand the community, to get surveys, and interviews, and help understand the patient perspective. And none of those are really made to fit together into one holistic document. So what we're learning on a daily basis is how do you take surveys and interviews and things like that from different organizations and bring them together into a more holistic perspective? I hope that someday soon I'll be able to come back to a meeting like this and tell you some of those lessons learned. We're currently in that work.

[01:34:30] The third lesson, and I think something that is really important for all rare disease, is that the question changes the answer. And what I mean by that is that a single risk tolerance number for HD would be misleading. To be useful, a preference study has to ask about stage, about the kind of treatment, and about certainty of benefit. So that's how we're designing any new work that we're doing is incorporating all of that, and it's a lot. Especially to be product diagnostic, it's a lot of questions to ask. And you have to ask them [01:35:00] in the right way and design it in a way that the community can understand and are informed so they can make their own informed choices. The fourth lesson, and maybe the most important, is that coming together as patient advocacy organizations itself is the work. In rare disease, as we all know, time and resources are incredibly limited. Meetings like this are so important to connect with others to share resources, contacts, information, and anything you might have to help advance the patient [01:35:30] voice in rare disease.

So to close, I just want to come back to that question of, it depends, in benefit risk information. For a long time, that answer has felt like a problem, something that's too messy to bring into a regulatory setting, but our community is betting that is actually the most important information we can offer. It depends, is data if we measure it carefully. So I just want to leave this room because I'm here to learn as much as I'm here to maybe give you some insight with a question and it's [01:36:00] actually partially been answered already. And that's, when a community itself comes forward with preference data that is stratified, rigorous, and not tied to any one product, how should it enter the conversation early enough and clearly enough so that it actually shapes decisions it was built to inform? Thanks.

Susan C. Winckler:

Thank you so much to Terry, to Tracy, to Emily. What [01:36:30] powerful stories and examples from very different perspectives. And as I heard Emily, I was thinking that in our conversations about gathering the patient voice that there's times when that patient voice will be a chorus or almost an orchestra because of the heterogeneity. So thank you so much for that. It is now time for a short break. And so we will be back and we will start up at 2:55 with a [01:37:00] lot more chairs on this stage. So, thank you so much. Enjoy the break.

Panel Discussion: Advancing the Patient Voice in Medical Product Development: Reflections and Opportunities

Allyson Berent, DVM, Chief Science Officer, Foundation for Angelman Syndrome Therapeutics
Michelle Campbell, MS, PhD, Associate Director for Stakeholder Engagement and Clinical Outcomes, Office of Neuroscience, Office of New Drugs, CDER, FDA
Donald "DJ" Carlino, Manager, US Advocacy, Novocure
Tom Croce, BSPharm, Vice President, Global Patient Advocacy & Engagement, Jazz Pharmaceuticals
Mona Elmacken, MD, Lead Physician, Malignant Hematology Branch, Division of Clinical Evaluation Hematology, Office of Clinical Evaluation, Office of Therapeutic Products, CBER, FDA
Courtney Lias, PhD, Director, Office of In Vitro Diagnostics, Office of Product Evaluation and Quality, CDRH, FDA
Jenn McNary, Principal, Co-Founder, Canary Advisors
Tamar Thompson, MS, Vice President Patient Experience & Insights, Alexion, AstraZeneca Rare Disease
Ashley Valentine, MRes, Co-founder & CEO, Sick Cells

Susan C. Winckler:

See, look how quiet you got this time. Thank you, all. We are ready to kick back off. And so what a collection of people we have on the stage. Thank you for joining us for this conversation. And I will say we are going to introduce everyone as we give them their first voice. If you are someone who was just really pinned to the agenda and you say, "This panel looks slightly [01:37:30] different," it does. We had one panelist who is ill and so her colleague Donald, or DJ Carlino, has stepped in. So thank you DJ for stepping in on eight hours notice. We appreciate that.

So the panel that you have assembled on the stage is going to allow us to hear from three essential parts of the medical product development ecosystem. So we have the patient advocacy community, regulated industry, and FDA [01:38:00] itself. And I am looking forward to this group. So we're going to just kick it off right away. I want to start with one of our patient voices and I'm going to start at that end of the panel. So CEO Valentine, would you describe what good looks like in terms of intentionally gathering and using the voice of the patient from your experience as co-founder and CEO of Sick Cells?

Ashley Valentine:

Sure. Yeah. So I'm Ashley Valentine. I'm a co-founder [01:38:30] and CEO of Sick Cells. And before answering that question, just a little bit about Sick Cells. We're a national advocacy organization for sickle cell disease and the other co-founder is my brother Marqus Valentine. So he passed away in 2020 from sickle cell, but he lived 36 years with sickle cell disease. And the last time I was at FDA, or we as a family was at FDA, was in 2014 when Marqus was part of the first and currently only PFDD meeting for sickle cell disease. And that meeting is [01:39:00] fundamentally the most important, one of the most important factors in drug development for sickle cell disease. Prior to that 2014 meeting no one asked the sickle cell community, "What do you need?" We in the community didn't know each other. We didn't have a community for all intents and purposes. We didn't even know we were a rare disease.

And we'll never forget that meeting because it was February, it was freezing. If anyone knows sickle cell, we're really impacted by the weather. So lots of people, including my brother, came to this meeting and then immediately went home to the hospital. But [01:39:30] that meeting was so important because what we were able to do was talk about just, "There aren't resources for this community," and it really undid a misconception about sickle cell that we don't participate in clinical trials. So off of that meeting though, drug development took off for the sickle cell disease space. And so the question is, what does good look like? And some of the first companies to really create solutions for sickle cell disease and get some of our first approvals, they really did a [01:40:00] great job.

And one of the companies in particular is what I consider the standard to this day. They hired at their company people in all sorts of level, all the way leadership down to community engagement teams, to admin that looked like the people that they were studying. They really, really invested money into the sickle cell population and to the community members. They leveled the playing field between the patient population, the provider community, and they understood that in a community like ours that's underrepresented, misunderstood, coming from a minority population that information does not flow [01:40:30] provider down to a patient. Patients weren't being presented clinical trials. So what this company did was they brought the information to the patients and the community often heard about updates first, they were involved in the clinical trial design. The company was sending people out into the field, participating in walks, in church meetings, and all of these things so that information about clinical trials could be brought to providers and that's how we enrolled many participants.

So whenever I meet new companies I always say, "Study that one because they did [01:41:00] it right." And that's really the fortunate opportunity we had when we first started in drug development.

Susan C. Winckler:

Yeah. Excellent example in helping us think about going to, and reflecting, and listening.

All right, let's add another dimension of the patient voice. We have another co-founder on the stage. And actually this might be my favorite title, Principal McNary. You have both direct patient engagement experience and experience as an advisor to other rare disease groups. [01:41:30] So add to our developing picture of successful interaction to gather and use the voice of patients.

Jennifer McNary:

Sure. And it'll be no surprise to anybody that knows me that I use a phone a friend. I take this honor of representing patient voices very seriously. And so I never get onto a stage without asking some people that I consider to be the though leaders in this space to help me weigh in. So you don't just get my opinions here.

I think [01:42:00] what we know, and what we've learned, and what we've been saying is that we've become very successful in utilizing, we the community has become very successful in utilizing the mechanisms mentioned earlier. We know them, we use them. I work with biotech companies, I work with patient advocacy. We do listening sessions in our sleep, we do EL-PFDD meetings, we know that's the first start. I think even the advisory committee meetings, the OPH, rich with data. It's very interesting and people find it useful. [01:42:30] It's the using or documentation of the utilization that I think is lacking here. And so I think that's the important part of this. There's little known about how those patient experiences are utilized, how the preference data is utilized. And I think it's not the usual route, but I do think we're also finding real benefit in that direct communication.

We heard on the stage this morning that it's really important for folks to have this bidirectional communication, [01:43:00] a conversation, not just to be talked at, not just to read a document that exists, but to be able to come and sit in a room. And so I think we need to do more of that because it's what I have seen be the most impactful kind of engagement, though it's not the easiest to find. You don't have a mechanism to request that type of engagement, but when it happens, it's incredibly powerful. When you have patients sitting down with regulators and decision makers, and [01:43:30] they are able to truly convey in real time what's necessary, what's needed, what their experiences are, what their experiences are not, what their preferences are. When they're able to have that conversation and hear back, not just somebody dialed into a Zoom listening to a meeting, not just somebody taking notes in an audience, and not just somebody reading a document. But when there's an actual conversation, that's where it works.

So the other thing that I was really interested in hearing this morning, and [01:44:00] I think that it's true, and I think we're doing it well, is that we do need to have patient experience data throughout. It's not just a snapshot, as was said this morning, I think Robyn Bent said that very well. And so there are mechanisms to do it all the way up to that post-market. And I think that one of the things that we really need to zero in on in this conversation today is that, how are we getting real time feedback? That's something that's definitely lacking.

Susan C. Winckler:

So that's a great point in illustrating [01:44:30] that the medical product development ecosystem doesn't end at product approval. Obviously there are many communities seeking even that, but once on the market, there's part of that innovation cycle and continuing to understand and hear the voice of the patient post-approval. Thank you.

So let's pivot and turn to the perspective of regulated industry. So I'll turn first to Dr. Croce. You're vice president of Global Patient Advocacy [01:45:00] and Engagement at Jazz Pharmaceuticals. How do you describe success for patient interaction?

Thomas Croce:

So, great question and thank you for the opportunity to be here. I heard Dr. Davis, Dr. Mikhail this morning talk about early and often, talk about throughout. It's very similar on the inside of a company, right? The opportunity, and I get asked the question all the time, "So when should we engage?" And my question back is, "What do you want to know and why do [01:45:30] you want to know it?" Because we've engaged preclinical as we're starting to think about, "Okay, what do we need to know in the way of natural history, patient journey, et cetera?" All the way through. And I'm glad someone brought up post-marketing because we have a recent example. We had a drug approved and we brought the patient input into all the customer facing materials that we're going to develop. And boy, did we almost get it wrong. But the input we got really [01:46:00] helped us to shift our thinking and really provide a better product for the patient and a better suite of services.

So I like to look at it from that perspective of what's the why, and then I can tell you when and how. We have no problem getting input from patients, caregivers, and advocates. And I like to use the three because I think while they represent a different perspective, they're incredibly complimentary. And so when we try to do it, what we try to do is purpose driven, "What do we want to know? When do we need to know it? [01:46:30] How are we engaging along the continuum?" And what really I have found so interesting is after the second meeting or so all the filters come down, and when we pose an idea or a concept instead of getting, "Oh, that's interesting," we get, "Did you lose sleep the night before? What are you thinking?" Which is the honest feedback we want-

Susan C. Winckler:

So you get candor-

Thomas Croce:

Exactly, exactly.

Susan C. Winckler:

... as they get accustomed.

Thomas Croce:

What's really bubbled up from the patient community over the last several years is, "We're happy to do this, [01:47:00] we want to understand what you do with it." So that, I think somebody mentioned, that bidirectional piece is critical for us, for the patient communities to continue to do this. And one of the biases you get from sometimes internally is, "Well, we couldn't use everything, so we didn't want to offend anybody." And my argument is, "Listen, let's go back, tell them what we did, let's tell them what we didn't do, and let's tell them why." Because now we have an opportunity to educate [01:47:30] and maybe it's going to be a regulatory issue and maybe it's going to be a flat out business issue.

Now, I think somebody raised it in earlier side conversation we were having about getting patted on the head as an advocate. We don't always respect our advocates and patients on the same level that we do our clinicians, our payers, et cetera. So you asked what success looks like. To me, the third pillar of this to me [01:48:00] is, "How are we developing medicines with patients, not for them? How are they part of our process?" And again, it's a little bit of a bias on my part, but most companies will say "We are hyper-focused on our customers and patients, which means we're not considering our patients a customer. So how do we get our thinking to where the patient is a customer? They are the end user of our product. They are the ones that, as we design our services, as we design [01:48:30] our products, we should not have them in mind, we should have them at the table. That's, to me, what success looks like.

Susan C. Winckler:

Yeah. All right. So we're thinking post-market at the table and incorporating throughout with folks who can have that authentic conversation. So let me turn, Dr. Thompson, to you. So you have a title at Alexion that's similar to Tom's, at least in concept, but with an emphasis on patient experience and insights. So share [01:49:00] how your organization moves from gathering that patient input, so perhaps having some of the conversations that we've been talking about, to generating credible patient insights and data to meaningfully inform product development.

Tamar Thompson:

Yeah. Susan, thank you so much. And thank you for allowing us to be here and have these conversations today. I want to thank everybody on this panel, what an extraordinary group that you've put together. And thank you for promoting me to doctor. That is actually my husband, Dr. Thompson. [01:49:30] So I think what good looks like from my standpoint, I lead patient experience and insights, and that's an odd title maybe. People kind of think it may be patient advocacy. But what good looks like to me is STARs and LEAPs, and I'll explain what that means. So we have a program at Alexion called Solutions to Accelerate Results for Patients. And we also have a program called, because we only call it LEAP [01:50:00] all the time, so I forget the acronym and what it means, but Learn, Evolve, Activate for Patients. So these are two programs that we put together and pharma loves a good acronym and marketing titles and-

Susan C. Winckler:

So do regulators. It's fine. Yes.

Tamar Thompson:

And so do the regulators. But these are meaningful programs that have been put in place to actually engage. And thank you for teeing this up for me, Jen, I really appreciate you. But these are meaningful programs that actually engage the patient community. So the STAR program, [01:50:30] for those of us who are in DC and love a good think tank, is kind of that. It's an environment where we bring our patient communities together around a disease state or any therapeutic area that we are in. And we bring the patient community, but we also bring the provider community, and we also bring, in some cases, we'd love to bring the policy driving community and others. So if you think in Europe, HTA and other areas, so we want to bring those into the table as well. And we do generate insights [01:51:00] from those

discussions, they are recorded sessions, but those insights then are leveraged across the drug development continuum.

So these programs, I'll give an example of what STAR means to us. When we did a STAR for GMG, an asset that we have recently launched, a second generation of our product in the US, we heard through the STAR program from the patient community that they didn't want a [01:51:30] traditional syringe, they'd rather have an autoinjector. Most companies don't go straight to autoinjector. The reason that the patient community wanted the autoinjector, think about, it's GMG, the difficulty in trying to inject. And so we listened to that. That became a very challenging thing to pivot and do, but guess what? We did it. Because the patient said they wanted it, and they needed it, and that's what's now in market.

And so those sessions are meaningful. [01:52:00] We listen to the patients in early drug development when we're looking to develop the clinical trial protocol design. And so we've had instances where we are thinking about biopsies and maybe taking two samples, and the patients are, "Are you crazy? This organ is important to me and you're not getting two samples of it. So I've named it." And things of that nature. So, "Okay, how do you design a clinical trial protocol that responds to that?" But we also take those same insights and then [01:52:30] we expand upon that for at launch. And then we take that insight and leverage it in other countries as we launch and then beyond.

So we do take that opportunity to build meaningful insights. We store them, we've turned them into podcasts. So when new people join, we're like, "Hey, here's your podcast. Walk your dog and listen to it," so that they can get up to speed and not having to go back to the community and regain those [01:53:00] insights. But then we do go back to the community to refresh, because as we learn more we want to engage the patient community in that concept as well.

LEAP is a very different, it's much more of an internally faced program. Because we find that when people join pharma companies, not all of us are patient centric and that's okay, we'll teach you that. So the way that we teach you that is that we have a program that as you join the company, we help you to understand [01:53:30] the patient journey. And we do LEAPs in all of our disease states. So if you're joining the company, now we are part of AstraZeneca. If you're joining in oncology or if you're joining in rare disease, there are opportunities for you. If you are in an area where you're not having the opportunities that I have to engage with a patient every day, that you can learn about the fact of, "In this disease state, on average, it takes about 10 years to get a diagnosis. In this disease state, they see [01:54:00] seven different specialists, et cetera, et cetera."

And so no matter what your job is, whether it's an admin, who are super important, or whether you are the CEO, you're going to get that programmatic patient centricity as well to help inform the way that we do our work.

Susan C. Winckler:

Really helpful. And now we have two new acronyms to think about and how we incorporate it.

So let's do our third perspective in the group. So Dr. Lias, one of the common questions we hear [01:54:30] when discussing the voice of the patient is how regulators use that information. I think you already heard it from other panelists. And a question about what is most helpful. So would you share your thoughts from the perspective directing the Office of In Vitro Diagnostic at CDRH?

Dr. Courtney Lias:

Yes. And thank you for having us up here. I'm Courtney Lias. I'm the director of the Office of In Vitro Diagnostic at CDRH. And in my office we have a lot of rare disease diagnostic tests. In our center, we have a lot of devices useful [01:55:00] for rare diseases. And what I'm going to share with you today is a story that's not a rare disease story, but is applicable and I think really illustrates the point of how we might use patient preference information in any of the products we regulate, including in rare diseases. So we also work in diabetes, and diabetes has both rare and non-rare users, but a lot of the companies that come in for us are non-rare users.

Several years ago, we were working with a big consortium [01:55:30] developing autonomous insulin dosing products. So these were products meant to take glucose data from a sensor and turn it into automated insulin doses. And there was a lot of engagement from clinicians and from academic researchers, all talking about how insulin is a dangerous drug that can cause death and serious injury if a product that we're dosing it autonomously were to malfunction. There was a lot of focus on how risky these products were. But when we talked to the patients, what we heard was very [01:56:00] different than that. They didn't care as much as us in our discussions talking about keeping patients safe, they didn't care as much about those risks. Because what we heard from them is, "We're at risk every day. I'm at risk when I go to sleep. I'm at risk when I'm trying to calculate my insulin dose." And so it really was an epiphany in perspective for us at FDA to hear about how much risk those patients were willing to tolerate.

And what we did with that information is it really turned around [01:56:30] how we worked with companies toward getting these products to patients faster. And so we were able to streamline a clinical trial. We were able to adjust our thinking about the uncertainties that we could accept in risk in the approval process. And I believe that the process of talking and listening to patients in this area got that product to the patients two to three years earlier. Now we have a lot of those products on the market and it really directs what we also heard [01:57:00] from patients. What they care about is something that makes their lives easier, that helps them deal with the unchanging burden of having to think about their diabetes every day. And so those epiphanies are really what can help.

So what do we need to hear? We need to know what's important to you. We need to know what's not important to you. I think it was very helpful to hear the Huntington's disease perspective. Today we are in an era where there's a lot of discussion about newborn screening sequencing [01:57:30] of babies at birth. What do patients want to know about rare diseases that they might find at that stage? What do they not want to know? I think that information is really helpful, not only to FDA, but to the entire public health community in making those choices.

Susan C. Winckler:

Yeah, that's a great observation as we think about, we often think about treatments, but also then thinking there in diagnostics and what do you want to know when? And I believe the phrase is, it depends, as we think through that. So really [01:58:00] helpful example in saying this is what you heard and then how that affected the work of the center in thinking about the review process and the trials. So I want to turn to your colleague right next to you. So Dr. Elmacken, is the perspective the same or different? You sit at CBER in the Oncology Center of Excellence as lead physician. Similarities, differences?

Dr. Mona Elmacken: [01:58:30]

I would say similar.

Susan C. Winckler:

It should. Keep going.

Dr. Mona Elmacken:

Yeah. So I would say very similar. So I joined the FDA seven years ago, so it's not a very long time. However, I would just say over the last few years, I'm a hematologist by training, oncologist hematologist by training. So there is something new development that is called cell and gene therapies, CAR T-cell therapies for cancer. And initially all of those [01:59:00] therapies were administered inpatient, and patients had to stay in the hospital for two weeks because of the toxicities. Then the patients came and complained, "We have families, we can't have companions." So we started allowing outpatient infusions. So now it became a very different, it's a one day and go home. And then also where you get this infusion. So initially there was this something called REMS program. REMS [01:59:30] stands for Risk Management and-

Susan C. Winckler:

Risk Evaluation-

Mona Elmacken:

Evaluation. Yeah. And then for that, there were very pre-specified hospitals that were allowed to administer those infusions. And then the physicians started complaining because that's lots of training and time taken from the physicians, and nursing, and everybody. And the patients started complaining. So we had [02:00:00] sponsors collect some information about safety and we removed the REMS last year. And now the issue is now there is access. So you can go into a rural area in the middle of the country, you don't need to be at Yale or Harvard to receive a CAR T-cell therapy. You can be anywhere in the country and most of the centers are allowed to give those therapies. So I would say it's very similar.

One [02:00:30] thing that I think is very underutilized because I heard somebody saying that it's not bidirectional, but for example, in hematology oncology, we always write at the end, we have something called end of Phase 1 or end of Phase 2 meetings with sponsors, where we invite sponsors to come and discuss with us the registrational studies before [02:01:00] they initiate the studies. And we always tell the sponsors, "We encourage you to invite patients to the meetings." However, I have never seen one.

Susan C. Winckler:

Oh.

Dr. Mona Elmacken:

I think it's-

Susan C. Winckler:

So you have an empty chair there-

Dr. Mona Elmacken:

Yeah.

Susan C. Winckler:

... at the meeting.

Dr. Mona Elmacken:

I think it's underutilized. Patients can have an opportunity, at the stage of designing a registrational study, to say their opinion. Whether we take it or not, that's the difference. We will think about it, but we [02:01:30] should definitely consider, we love to consider it. Post-marketing, one issue is for the safety and adverse events, we have changed labels and put black box labels based on reportings that we get from patients. We have removed mandates for children, like pediatric studies that had to be only initiated [02:02:00] after adult studies are completed. That is gone out of the window based on families, parents coming and saying, "We can't wait for the adult studies to be completed."

Very recently, like last month or some months before, we had another patient hearing session because after cell and gene therapies there is a 15-year-long follow-up and sponsors are complaining. So we though patients will be complaining. Unanimously, [02:02:30] all patients said, "It's once a year. I still want to be seen by my doctor. I still want to get that." We expected completely the opposite. "We want to be seen. We want to have this assurance, 'You don't have your cancer, go home and come back next year.'" The only things they said was, "We would love to be seen by another doctor that communicates with the one who is holding the study." So just to simplify life. But, yeah.

Susan C. Winckler: [02:03:00]

Yeah. Really helpful. And again, kind of surprised. I guess one of the things we're hearing is that sometimes you're surprised.

Dr. Mona Elmacken:

Correct. We were surprised.

Susan C. Winckler:

Yes. All right. So one of the common questions in efforts to gather the patient voice is about timing, and some of you have talked about that. But I want to turn to you, Dr. Berent. In your experience as chief science officer at the Foundation for Angelman Syndrome Therapeutics, is there a right time or a wrong time to seek patient input?

Dr. Allyson Berent: [02:03:30]

Well, thank you. And thanks for the invitation for being here to the FDA and to Reagan-Udall. I'm humbled to be able to share our experience and what we think is important certainly as a community. Firstly, I'd like to just share my experience with multiple hats, not just as the CSO of the foundation, but I think it's important because I look at this in many different angles. Firstly, I'm a clinician scientist and I've been the PI in multiple clinical trials. And I'm the co-director of a biomarker and outcome measures consortium that's pre-competitive that really brings together industry regulators, [02:04:00] researchers, clinicians, to truly get the patient voice to the table as we think about endpoints, clinical trial designs, developing biomarkers, what matters, what's meaningful. And I also am part of the development team for an AAV gene therapy, a hematopoietic stem cell gene therapy, and a CRISPR gene editor. So I understand the industry side as well as we think about nonclinical and clinical development and what it takes and when we need input in order to get there to get to patients, not only to get to animals. And so the most [02:04:30] important hat that I wear though is actually I'm the mother to a beautiful little girl and she lives with Angelman syndrome and her name is Quincy because I think the north star is that little face and it's that little girl. And similar to Terry, I think it's more important that we're here today to not only share when the patient voice should be heard, but what that patient voice is and that lived experience.

And I think the answer to the question is the wrong answer is once, the right answer is constantly. And I think in terms of when you seek patient input. [02:05:00] And I think it's important to recognize that it evolves with time. It's important to recognize that that first point in which you're getting patient input is generally when you're designing a clinical trial or you're in the preclinical phases thinking about a clinical trial. So we get patient input, we talk to patients, we think about what they want, we work toward what are the meaningful endpoints, what are the meaningful symptoms and how do we develop endpoints for them? And what I can tell you is that that changes over time and it iterates because in my own lived experience, [02:05:30] when I was asked this question, what did I want for my five-year-old daughter who was about to enter a clinical trial?

I wanted the world. I wanted my nonverbal child who sleeps two hours a night, who can't feed herself, who cannot live an independent life for the rest of her life, cannot speak a single word and who cannot even respond to her name. What did I want for this beautiful little girl that has a non-degenerative neurodevelopmental disorder? So she will be alive for the next 50 to 70 years. What did I want for her? I wanted everything. I wanted conversational [02:06:00] English. I wanted her to go to college. I wanted her to get married. I want her to have kids. I want her to live an independent life and I don't want her to rely on us for the rest of it. That's what I want, right? That's a fact. Then she goes on a drug and in six months, what did we get? We got a child who when I said, "Stop," didn't cross the street in Manhattan where we live and she looked at me and stopped on the corner.

I have a child who developed a finger point because now she can point at her iPad and communicate expressively [02:06:30] on her iPad. And I have a child who can feed herself at a table. And ask me 18 months into the clinical trial, "What do we have?" I have a child who can independently swim, the leading cause of death being accidental drowning in our community. I have a child who can communicate her needs and her wants and the most important word on her talker is help because she can finally advocate for herself. So I want you to know how many of those are collected on that primary endpoint that we all are working so hard for, that's the gold standard clinical [02:07:00] reported outcome measure, that [inaudible 02:07:04]. How many of those things are captured? Almost none. How many of them are captured on a PRO, which is a little bit less than the standard?

Almost all of them. And so when we think about what I wanted when I was asked the first time, but what we got, which is transformative and it's everything to our family, maybe not to all families, but to ours, what I can tell you is that we need to iterate because if we didn't ask again after [02:07:30] 6 months and 18 months how we may need to manipulate what we're looking at as endpoints, manipulate and iterate on are we capturing the changes that we see, speaking to the clinicians, speaking to the PIs and speaking to the families and the patients affected, we're never going to get there. And we're really potentially going to throw out the baby with the bath water. We need to iterate every step of the way with the patients to say, "Are we capturing what they're experiencing and are they experiencing risk that's worth the benefit?"

[02:08:00] And if we only ask upfront, we're not going to get the story that we might receive in the end. And I think ultimately, we do ourselves a huge disservice if we don't iterate every time. And I think that's very important in rare disease, especially heterogeneous populations where we might think we know what they want, but what they get is a little bit different, but it's still meaningful and it needs to be measurable. And I think that's hugely, hugely important.

Susan C. Winckler:

Yeah. Thank you for sharing and the power [02:08:30] of thinking about that and the distinction of what we might have set as an aspiration and then the extraordinary... What is transformative.

Dr. Allyson Berent:

Just bring them to the table and ask the questions.

Susan C. Winckler:

Yeah. So I want to go to our... I was going to call you our stand-in. That's not fair. So DJ Carlino, thank you for joining us from your role as manager of strategic alliances at Novocure. So your [02:09:00] thoughts on... I know it's super hard to follow Allyson.

DJ Carlino:

I was going to say.

Susan C. Winckler:

Sorry about that. But your thought on the right time and does that time end?

DJ Carlino:

I mean, I think we've discussed it at length here. The right time is as early as possible and no, it doesn't end. So there's your short answer. I also come at this from a few different angles. I am a two-time AML cancer survivor [02:09:30] and I worked at the American Cancer Society for 12 years prior to my industry role. And so I have been the patient asking the questions. I've listened to the patients asking the questions and now I incorporate that into what we're trying to do at Novocure. And being a medical device is also a little bit nuanced as well. So for those of you who don't know Novocure, we're a

wearable device for oncology and so it's administered through tumor treating fields. And so patients are wearing this throughout [02:10:00] their day and their daily lives. And so incorporating what their voice is in how they're actually managing the symptoms, what they're doing with the device, what they're actually able to do with the device outside of a clinical setting is something that's very important. And we have a human factors lab that in our New Hampshire headquarters that is actively looking at these.

So they have connection points, which we call arrays. And so they can get itchy. They used to be heavy and part of the evolution [02:10:30] of the product line is that they made them lighter along with the bag that you carry it in. That's a nuisance to carry. And so how do we lighten that burden so that people actually want to use it and can benefit from it as well? But if they're not going to use it, the benefit isn't there. And so like I said, start with the short of yes, always and forever and as early as possible.

Susan C. Winckler:

Yeah. Excellent. Thank you. And someone [02:11:00] in this room is keeping track of whether I've gotten to all nine of you. I'm about to. So Dr. Campbell, thank you for joining us from Cedar's Office of Neuroscience in the Office of New Drugs. What is your thought on this? Now that you've had both DJ and Allyson answer everything, but from the regulator perspective, you are looking at it from a slightly different view.

Dr. Michelle Campbell:

It's a unique view I have. The [02:11:30] rare disease community knows this because they've heard me talk about this when I talk to them. I come to this when I came to FDA with a unique experience because I was a research coordinator. We won't tell you the years or the age.

Susan C. Winckler:

Not relevant.

Dr. Michelle Campbell:

Not relevant. In a children's hospital in a neurodevelopmental medicine clinic. So I was the one who was recruiting families for those trials and what those conversations were like. And so to me, naturally it was always, "Well, we should be talking to families. They know what's going on," because that's what happens in clinical medicine. They [02:12:00] are there every day. I'm surprised Allyson didn't talk about how at her meeting where I did push the KOLs and say, "Caregiver report is really important that we should be capturing."

Dr. Allyson Berent:

That's my next question.

Dr. Michelle Campbell:

That's your next question. But I think what's important, and hopefully I want to thank everyone who's here today, both in person and online, and then the opportunity coming up in two weeks to continue

this dialogue is really, how is the patient voice being incorporated into our everyday work? And I, as [02:12:30] someone who's been at the agency for now well over a decade, has seen it grow as Robin talked about from when the original program started with PFDD to where we are now. And there's a lot of folks in the room that were part of that journey, right? What was our original talks and where are we now? So there's been a great growth in this decade plus timeframe. But sadly, as Mona said, a week does not go by where I write to a sponsor in comments or at a meeting, "Have you talked to patients? Have [02:13:00] you talked to their families? This information would be important."

Or, we've been fortunate enough to have a patient listening session or a patient focused drug development meeting and have a voice of the patient report. So we've read what's going on to say, "Well, we understand the big concern from families is this. Have you considered capturing that in your clinical trial to support efficacy?" And so sometimes we're the ones having to say and push that as well. As [02:13:30] has been said, engagement, not only is it early and often, but it needs to be frequent and it is throughout that product life cycle. Where are you? I was recently in a meeting a couple weeks ago and there was a discussion about the capturing of data throughout this life cycle, including that post-market space. And that is also important because that can inform us in safety and maybe future indication development work. It's going to inform other key stakeholders that aren't here in the room today with us, but are critical. We know, we hear this from families, [02:14:00] access to care, payers. This data needs to be collected.

I would say I'm seeing a really great desire from families, and I shouldn't say as a grassroots effort because it's not grassroots anymore. It is systematic. It is with rigor and it is being able to put together good research and what needs to be done. And we often get a lot of questions about, "Are we capturing the right thing? What should we do?" And I think [02:14:30] what you are seeing is where there's opportunities to try to provide as much single quick high level advice we can give to give thoughts that can hopefully advance good quality information and data collection that is happening outside of that IND or in the device settings, the data that they need as well. All three of our centers are touched by rare diseases in many ways. And so please do, and depending on which center you engage with, [02:15:00] come talk to us earlier.

And really, I have no problem in a phase one first in human pre-IND meeting where if you're already thinking about that pivotal trial design, talking about stuff, we will start providing that advice then. We will start thinking about what needs to be done. Before I came over and walked over from my office today, I've spent all day in rare disease. I've probably worked on four different programs and was literally sitting there going, "What can we actually measure? What will work? [02:15:30] What can't work?" And those are our everyday conversations. And so I know sometimes it's hard to see how we use that information because the end product for us is maybe a marketing application decision, but we are every day using the information that is captured and it starts with the information we learn from you.

Susan C. Winckler:

Yeah. Yeah. Thank you. And thank you for the work that you were doing this morning and earlier this afternoon before you came to the panel. And helpful just to remind us of thinking about [02:16:00] from the regulatory perspective, how you look at that information throughout the life cycle. So I'm going to do a little bit of grouping now. This one, just for the heads-up, it's going to Tamar, Tom and DJ. So your organizations have some similarities and some differences. So Tom, you're at a solely rare disease company. Tamar, as you noted, you're at the rare disease arm of a larger company. And DJ, you're at a company that has multiple products, one of which [02:16:30] is rare disease. So do those different

market positions translate into something differently with the patient voice topic? And I know you can't answer for each other. So DJ, you get to start.

DJ Carlino:

That's an honor. Thank you. But I think in the basic sense, no, the patient voice should always still be at the center, whether it's rare disease [02:17:00] or not. I think the questions differ. That's the difference in terms of what do some of these rare disease patients really want out of a treatment? Overall survival is usually the end all be all, but is that really what they're looking for? Allyson really eloquently put it, that's not always what they're looking for specifically. And I think taking that into account can really shape the product [02:17:30] and what people want to utilize it for.

Susan C. Winckler:

Tamar, thoughts?

Tamar Thompson:

I mean, in theory and philosophy, of course we want the patient's voice at the center of everything that we do. I will speak for the rare disease unit and I'm incredibly fortunate to get to have a microphone and be the amplifier for the patient community for which I represent. And what is different there is that the patients often know more than we do about the disease state. [02:18:00] And that is not always true in other sciences and larger chronic diseases and conditions. So we have no choice. The way that we look at life is that if we're going into a new therapeutic area or if we have an opportunity, we bring the patient into brand forums or other things because oftentimes our patient community, 98% of the time, not just often, know more than we do when we're starting in that space. [02:18:30] And so we have to start there.

And when you're building upon data and science and looking at it differently, your lens on patient centricity may be different and where the role of the patient voice is in that continuum. But on the rare side, this is the reason. I'd love to say that we were innovative and though forward 30 years ago to include the patient voice because we knew this was going to happen, but no, we didn't. We just had no choice. [02:19:00] The patient has to be at the table.

Susan C. Winckler:

Anything?

Thomas Croce:

No. So I agree with all that. I think one of the things, and probably Tamar experiences as well is in a... I've worked in bigger companies, in this size company, less hearts and minds to convince, better ability to put a system in place for this so that it is consistent, there's accountability and it's utilized. And I think the only other piece is [02:19:30] in these small conditions, sometimes it's the only place we have to go for information. You can't call IQVIA like you can in diabetes and get a download, right? You've got to turn to the community, you've got to turn to their registries, you've got to turn to some of the work that they've done. And that's where we get a lot of our information in these small population of patients.

Susan C. Winckler:

Yeah. Very helpful. So let's go back to our regulators and Dr. Campbell, you already started answering this, but answer [02:20:00] it with a little more context. How do you all use the patient voice in your work? You've given us some examples, but this really is the question that is asked again and again and again.

Dr. Michelle Campbell:

It is. It really is. And when I do have the opportunity to provide open remarks at external patient drug development meetings, sometimes there's a prep with the patient group and Allyson has experienced this with us is, "Hey..." [02:20:30] Here's, I know, the common questions we hear, is, "How do we use this information?" It's the number one question and it's a fair question because that's what you want to know. And I think Tom said it great because in the end, we're here for you. We are here for you, we're here for the families. And so you should ask how we use this information. So the hard part is, is we may not be able to show how we use it if we're able to make a positive regulatory decision. And so that may be [02:21:00] some time from when that engagement opportunity occurred. So what I try to explain what we do is how is it in the everyday?

So as I mentioned, we can leverage voice of the patient reports or patient listening sessions that we may have had into our everyday advice we give. And I can give you an example. So we had a patient listening session where there was a hallmark primary symptom, carnal symptom, it's in the name of the disease type thing. And so we're listening to the patients and their families and their lived experience, [02:21:30] and this is a genetic based disease. So they're talking about this entire family experience, that they're not the first member of their family. And we're listening and we're hearing them talk about other symptoms that they deal with on an everyday basis. And behind the scenes, we're all questioning each other going, "Are we getting this information in clinical trials? Are we seeing this?" Because we know how to measure this. We actually know how to measure what they're describing to us in a reliable way.

[02:22:00] We have scales, we know how to interpret it, we know what to do. And so at the end, when we were thinking and we only ask questions, we brought this up and said, "Hey, are you guys capturing this? We heard a lot about this. We know what to do with this. This is informative to us. This is part of your lived experience." And they said, "Well, no." And they've since added it to their natural history because we're like, "This is important. It's a missed thing." No one is coming and telling us that is [02:22:30] important, but they are clearly telling us in their lived experience is a very impactful aspect of disease. And so we should be capturing that.

Susan C. Winckler: So the teams chat behind the scenes.

Dr. Michelle Campbell:

Those behind the scenes conversations, this happens all the time in our PFDD meetings where we're sitting there going, "Hmm, Someone said that if they could just maintain finger..." It was one of the muscular dystrophies. I think it was congenital muscular dystrophy. I can't remember. But I remember in one of them, they were saying, "If I can just keep the movement of my finger, I can operate [02:23:00] my wheelchair. That's all I really care about, if I can do this." And I'm sitting there going, "Okay, how can we do this? How can we measure this? How do we need to do this?" And there was this behind the

scenes... Because if we got this question to come in, if someone was to come in the program, we would have a way of thinking about what to do. Or in another meeting we've been to where they've talked about, "If I can just stand without falling for two minutes, I can microwave my dinner and be able to feed myself. I can actually not [02:23:30] need assistance in preparing a meal." Those are-

Susan C. Winckler:

The ability to turn over where-

Michelle Campbell:

Right. So we take those. There's a lot of behind the scenes conversations that happen. And then when we finally are able to have development in that space, we recall those conversations and we're like, "Hey, remember we heard this? How do you think this works?" And we actually may be the ones proposing a novel thing to be captured or a novel approach because of what we've learned from those patient interactions.

Susan C. Winckler: [02:24:00]

Yeah. Yeah. Fascinating. Dr. Lias.

Dr. Courtney Lias:

Yeah. And I love that story about how we can propose changes to trial design or data collection. Echoing back to the post-market question from earlier, I want to talk a little bit about how we can use this type of feedback to promote post-market improvements in devices to try to address these. So taking another sort of diabetes example, younger children with diabetes have caregivers. Their control is usually pretty good. Young adults get back to [02:24:30] being good, but teenagers are notoriously-

Susan C. Winckler:

I'm shocked.

Dr. Courtney Lias:

... awful.

Susan C. Winckler:

Shocked.

Dr. Courtney Lias:

And we learned from patients that a lot of it's embarrassment. They don't want to check their blood glucose in front of their friends. They don't want to be interacting with their insulin pumps or syringes in front of friends. Learning that, we contacted the companies, "Can you put this on their cell phones?" And what we learned from the patients is that they would value this particular type of advancement.

What we learned from companies is that they may have heard that information from patients, but [02:25:00] they thought we wouldn't accept it. And so they never approached us with it. And so this triangular discussion wasn't useful. So I encourage all patient groups, come directly to the source as well as talking to the companies about these things or get together in forums. Because when we learned this, we called up the companies and said, "Hey, we want these patients to be able to control their insulin pump with a phone. We want these teenagers to be able to act [02:25:30] cool and just look like they're checking social media when they're really checking their glucose."

And that did help. Parents reported to us afterwards, after we got them to implement that, that it really did help people use that better. Another one is parents were losing sleep at night because they had to set multiple alarms to get up and check their children to make sure they didn't die in the middle of the night. And how stressful would that be to every night not to get a good night's sleep as a caregiver? Same thing. We just put the alarm on the phone, but the company didn't realize [02:26:00] we would accept it. And so we sort of said, "That sounds like an easy fix." That was one of those moments where you're sitting there and in our minds, we're in the Teams chat going, "That sounds really easy." And so we were able to push the companies to do that.

And so I think that's the type of thing that's kind of harder to capture sometimes is that these small pieces of feedback can sometimes help us help you in ways we wouldn't have imagined if we didn't learn it from patients.

Susan C. Winckler:

Yes. Yes. And this is where I want to say, remember, you can lean in [02:26:30] and jump in and put the microphone and start talking if you want to chime in and pull on this thread. But Dr. Elmacken.

Dr. Mona Elmacken:

Yeah, we definitely learn a lot from patients. So I can give you another example. So for CAR T-cell therapies and gene therapies, it's one-time infusion. So when we want randomized control trials, so we have this issue of patients don't want to enroll in the places in the hospitals [02:27:00] where they will be receiving chemo. If they are on the control arm, they want to get the CAR or they want the one-time infusion therapy. So led to different changes in trial design so you can allow crossover. So if the patient relapses or doesn't improve, so you always give the patients the option to get the other investigational therapy. [02:27:30] Though it messes up with overall survival data because it gets muddy when the patients... But the patient is more important than the clarity of the data at the end, you don't need to see if you have other endpoints that will show benefit, you can still do that because you want the patients to be enrolled on the study.

So you learn from what the patients want, what they need, [02:28:00] very importantly, how to change the study design. And you wouldn't know it unless the patient tells you, unless the study goes and no patient wants to enroll in it. So it becomes a little bit very important to hear from patients upfront and know what they want.

Susan C. Winckler:

And you brought up kind of this idea then of balancing and saying... Like you said, "It might be muddier. A muddier result, but that's okay."

Dr. Mona Elmacken:

So I'll give you an example for [02:28:30] one approval that we have. It's published. So we had one of the CAR T-cell therapies, randomized control trial for large cell lymphoma, very aggressive disease. Before the CAR T-cell therapies, patients wouldn't survive long. And now you have 85 to 90% response rate with the CAR-Ts. When you have a randomized control trial, you can find something called event-free survival [02:29:00] and progression-free survival. You can see the curve is very well split. You can see 20, 30% benefit. But when it gets to overall survival, because you allowed crossover, the people who crossed over, you are not counting the events anymore. It's only overall survival. They are surviving. They survived because they received the CAR-T, but... So the curve, there is still a difference in improvement because [02:29:30] they received it earlier, but it was not statistically significant. But you saw the statistical significance with events-free survival, you saw the statistical significance with progression-free survival. So response rate were much better. So you change the trial design, you get approvals based on what's really good for the patients, what really helps them survive.

Susan C. Winckler:

Yeah, the ability to adapt there. So we've veered into our next section [02:30:00] that we wanted to talk anyway. Let's talk endpoints. And you introduced this so well, Allyson, as we think about what matters, and we're just talking about adaptation there. So where have you seen success or perhaps not so much success in making sure endpoints are both patient-centered and regulatorily acceptable? And our patient advocacy groups get to jump on this one first. So let's go Allyson, Ashley, Jen.

Dr. Allyson Berent: [02:30:30]

Great. So happy to start here and I'll take what Dr. Davey said, which was be frank and be real. So I will do that because I'm always tasked with being provocative, so I'll be a little bit.

Susan C. Winckler:

We like that.

Dr. Allyson Berent:

I do too, because I think honesty is where we make progress, right? So we have to be provocative where we can. But what I would say is that when we think about endpoints and meaningfulness, we have to think about what are the symptoms and the impact of a disease. And every disease is going to be very, very different. Every rare disease is not only going to be different. Angelman's somewhat homogeneous compared to [02:31:00] other rare diseases. Many are very heterogeneous. So we need to understand what those symptoms are and what that looks like in different populations, but then also, how do we measure that and what are the endpoints we're going to use to measure that? And we put that hierarchy together and we put that list together. And then you have two options. You can use a validated or qualified measure that wasn't designed or developed for that disease and be fit for

purpose, or you can develop your own measure for that disease, which is probably far more appropriate.

But then you're left with this kind of [02:31:30] balance of... Well, if you use the existing measure and you're putting a round peg in a square hole, it has a regulatory path and maybe you're going to hit 10% of the gains on that measure, and maybe that's good enough, but a big risk. You design your own measure and maybe you're going to hit 90% of those gains. Like I described my daughter, Angelman defined and developed endpoints would have hit 90% of the things my daughter gained, but none of them are validated and none of them are qualified. And so therefore we're put [02:32:00] in a position to say, "Well, which do we use?" And so you really have to think about that. And so to Michelle's point, who's been amazing and the greatest advocate for rare disease truly, because she comes to these patient groups and tries to help support the next steps of what you do in these situations.

And so we had a patient focused listening session, which was wonderful in 2018. And it was... Someone at the FDA who stood at the table and designed a PIRO, a parent reported measure in communication abilities in nonverbal children for [02:32:30] Angelman syndrome. It was designed on a piece of paper in front of us by the FDA. They connected us to somebody to develop this measure. It's called the ORCA, the observer reported communication abilities measure for non-verbal children. And then we paid over a million dollars to get this validated for Angelman syndrome. We designed the whole thing. The FDA gave a grant for $2 million to develop it for 12 other neurodevelopmental disorders, a PIRO. So clearly there's agreement and people believe this has value. [02:33:00] But then what happens is we take this measure and we say... We put it in all the clinical trials. There were three Phase 1-2 ASO trials, now three Phase 3 ASO trials. But what do you do with it? We can put it through COA where some people might say, "That's where measures go to die." No offense, but that's what we hear.

Susan C. Winckler:

COA?

Dr. Allyson Berent:

The clinical outcomes-

Susan C. Winckler:

Clinical outcome assessment.

Dr. Allyson Berent:

Yeah. Assessments. Where if they go there, they can take a really long time to actually become qualified or validated. You can decide if you want to answer [02:33:30] that.

Dr. Michelle Campbell:

I'm just so uncomfortable right now.

Dr. Allyson Berent:

I love you so much. You hear that. So then you're advised by advisors, "Well, just put it through someone's IND because we have three INDs that are going forward and then you'll get feedback on the measure and you'll get it faster. It'll move faster and then maybe be incorporated." Okay, so we take that route because that's the advice we're given, but then the sponsor holds it. So the people that paid for it and developed it don't get the feedback of what the sponsor are getting in these INDs. So what happens is the measures sitting in these INDs [02:34:00] and there's feedback that we kind of get summaries on from the sponsor, and then we kind of get summaries on from regulators, and they're not the same feedback we're hearing. And so we're stagnant because we're waiting and we're waiting. Had we just gone down the co-route, we maybe would've been in a position in which we actually got the feedback by the people who developed the measure.

And this is just one example of how in rare disease... This is why people don't want to develop their own measures because they can just take too long and they may not get to where you need them as quickly as [02:34:30] you need them. So I think if we can put forward transparency, collaboration, every new measure needs to have people at the table, primarily people like Michelle, the regulators who really believe that they designed this. It's the right thing to do. And then industry, the feedback they're getting is what we're hearing, and then everyone can use it together transparently across the field. But that's where that lack of visibility from our vantage point makes it [02:35:00] really hard. So when you say, "Is it patient centered and... and regulatory acceptable?" The answer is, I don't know.

Susan C. Winckler:

Because you don't have the information.

Dr. Allyson Berent:

Because we don't have the information. And I think it is when I talk to regulators, but then you talk to industry and you hear, "Well, the regulator doesn't like," or, "That's not acceptable." And you're like, "But that's not what I'm hearing on this side." So, for me, I think it's really important that we take rare disease into a different direction where all endpoints developed for a rare disease [02:35:30] have patients at the table, particularly those who paid to develop them. And we move as quickly as we can to make them better if they're not acceptable. And we move as rigorously as we can so they're scientifically sound. And then we can maybe capture that 90% of what we're seeing in these clinical trials where these fit for purpose measures have been shown 1,150 gains in the Angelman phase one two clinical trials, 10% of them were captured on a ClinRO that turned out to be most people's primary endpoint.

[02:36:00] 10% of the gains were captured. And the PROs are on the lower end of the hierarchy, so they're really not being looked at. And so, I think we need to rethink this as rare disease because we're not diabetes and we're not hypertension. And so, there has to just be a different path.

Susan C. Winckler:

Right, because your data is rare.

Dr. Allyson Berent:

Exactly. Exactly.

Susan C. Winckler:

And then I think it also speaks to what we've heard throughout the day is the need for a conversation. That's one where you're saying [02:36:30] we've shared the voice and helped develop this because we then hear back from-

Dr. Allyson Berent:

And it's almost like we get more feedback from the regulators than we do from the industry that's using the measure we made. And we need to make sure that everyone's in a full circle about it because we want to make sure they're using it in the best way. Their interpretation of what the regulator said might be wrong. And we want to help support them to do the right thing and get their drugs approved that we believe might be working. So I think it's really important that transparency.

Susan C. Winckler:

Yeah.

Dr. Allyson Berent: [02:37:00]

I was provocative. You're welcome.

Susan C. Winckler:

Ashley, we talked a little bit about endpoints in our conversation leading up here. Share your thoughts. This is very helpful in saying need additional information, need to be hearing back about the performance, but share your thoughts on endpoints.

Ashley Valentine:

Sure. So, in the sickle cell space, I opened by saying we had that 2014 meeting, but since really that meeting, our endpoints have kind of been the same. [02:37:30] The science has outpaced the endpoints. The science has even outpaced standard of care. And the landscape has changed so much because now you have all these people invested in sickle cell disease. You have excitement in the community. We're being connected to each other, but we're almost beholden to these endpoints that is actually now capturing truly what's going on in the disease. So, when people first learn about sickle cell or honestly still this unawareness and stigma attached with the disease, we're kind of trapped [02:38:00] with this idea that sickle cell is just a disease about blood and just a disease about pain. But with investment comes now this innovation and researching the disease. And we're also learning now that there's different types of sickle cell disease, that different types of hemoglobin, it presents differently.

We're learning that there's inflammation. We're learning that fatigue is probably more impactful than pain. We're learning that there's different types of pain. Is it neuropathic pain? Is it bone pain? Is it chronic pain? Is it acute pain? And none of that is reflected [02:38:30] in most of the endpoints that are put forth for our clinical trials. And so, what we're seeing right now is exclusion criteria is a big issue

because either a lot of the population are not experiencing enough types of pain that's being captured for the trial. Inclusion criteria is also limiting because individuals are not visiting hospitals enough. And so, we're really tied to these endpoints and that's almost hindering our ability [02:39:00] to get drugs approved or enroll people in clinical trials. And then the other thing we're seeing about endpoints really comes back to study design. And so, while oftentimes the patient voice, the sickle cell voice is brought to the table, what we're finding is that some companies do it well, but a lot of companies still are struggling with translating what that voice means to a scientific setting.

I can give an example. I remember I was sitting in a meeting and they invite me to meetings all the time [02:39:30] and I like to level-set with everyone. I'm not that different. My mom's a nurse, my dad's an electrician. It just so happens that I listened enough that I can say words back. And so, they're telling me most people with sickle cell don't know how to talk about their disease. And I said, "Well, what do you mean?" And I'm here with the scientists and the sorts. And they say, "Well, the KPIs, the doctors told us that when they ask their patients what's their hemoglobin, are they anemic? Their patients don't know." But then in this next vein, they said, " [02:40:00] The patients only really want to talk about how tired they are." And so then my microphone was on, I didn't know it was on so I'm whispering all over to the side, to the side.

And they said, Ashley, "What do you think?" I said, "They're saying the same thing. It's up to you all to understand that if you're tired, you're anemic. If you can't go to school, you have low hemoglobin. If you're having to sit down because you can't stand up and wait for the school bus, that's because you're anemic and you have low hemoglobin or you have pain or you have hemolysis, destruction of red blood cells in your body happening." But because [02:40:30] that has been told to the team of scientists or the people creating endpoints, then that's what's being taken to regulatory. And so, what we're often seeing is that we still have this issue in the sickle cell community where that initial burden of stigma or misconception about us as a disease population, unless the people in-house working at these companies know how to spot that and can translate what's being said to the science, then our voice is not being taken [02:41:00] when building out study design or developing endpoints.

Susan C. Winckler:

What a powerful example of just thinking about when we're talking about endpoints, are we using the language that the patient might use to describe an endpoint of relevance?

Jennifer McNary:

Yeah.

Susan C. Winckler:

Jenn.

Jennifer McNary:

So, Allyson used the word stagnant and I just want you to know that I wrote stuck, so we're aligned there. When it comes to endpoints, I think we're stuck. And it's been long enough that people may not know how [02:41:30] I got to where I am. And I think it's really important because how I got to where I

am is because I was a mom who was watching my son in a clinical trial stop falling. And that was really important because he had Duchenne muscular dystrophy. And the biggest problem I saw at this late ambulatory phase of Duchenne muscular dystrophy were the constant and uncontrollable and heart-wrenching falls that these guys [02:42:00] have. They're walking along down the hallway and all of a sudden you just hear this thud and they fall. And if it's like my older son, you'd hear, "I'm okay," right after that.

And you know he's not and you'd have to go pick him up off the floor because they can't get back up. And oftentimes what keeps them from continuing to walk is a break as a result of those falls. So, these are really important, these falls. And my son was nine and a half when he entered a study and by 10 and a half, he wasn't falling anymore at all. And that was the same age [02:42:30] that his older brother was when he stopped walking entirely. And so, I was this mom who knew that one of my sons was getting better and his older brother who was not in this clinical trial was getting worse. And so, I needed to do something. And when I went into the clinic, I said, "Hey, he stopped falling." And they said, "Well, we're not collecting that, but let's see if he can walk further in six minutes than he used to be able to." And I said, "What does that matter? I don't care how far he can walk in six minutes, [02:43:00] but I care that he can walk for six minutes without falling."

And they said, "We're not capturing that, but let's see how fast he can walk." And so, I think that I didn't even know the name of what I was seeing. I didn't know that it was called an endpoint and I didn't say we should design some new endpoints. But what I did eventually say is all the kids in the study are seeing various changes and none of them are being captured. And so, I worked with this fine gentleman over here, James Valentine, giving you a shout-out, to try to collect some of [02:43:30] those things that weren't being captured in the clinical trial by doing some video interviews and talking to folks. And this was very new. This was a long time ago. Our drug was eventually approved in 2016 for Duchenne, but we started in 2012 when all of this stuff was just getting off the ground.

And so, the unfortunate thing though is that we're still really using the six-minute walk test as an endpoint in Duchenne. And I didn't think that that was applicable then and I [02:44:00] don't think it's applicable now. And so, we might very well be stuck. I think we're still not quite measuring falls. We're also not measuring finger usage. And let me just say that having been a mom who lived the entire date, dash, date of Duchenne, my oldest son died last year, I know that the dash was much more important than the last date. And so his quality of life was better [02:44:30] while he was alive because he was able to use his hands. He didn't live longer than maybe we expected him to. He died at 26, but because of some interventions that he was able to access, gene therapy, RNA-based therapy, it didn't make him live longer, but he was a guy that was a comedian. He was out on a stage holding a microphone.

He was out on a stage out at the bar at night having a beer. He was able to type on the computer. He was a real funny guy. He was able [02:45:00] to participate in lots of different things that were important to him because he could drive his wheelchair, to your point, Michelle. And because he could talk, he had a voice, he didn't have a trach. And so I think what we need to remember is that overall survival is not always the goal. I would love it if you were alive, but what I also love is in the last year of his life, because he had a therapy that worked. Worked, defining worked is really hard, but because [02:45:30] he had a therapy that worked, he went from not being able to eat to able to eat again, and that meant something to him.

So, I think the other piece that I like to share is that we don't always know what's going to hit, as Allyson said. And so, I am so tired of primary versus secondary endpoints that I could scream. I am reviewing a

protocol right now for a client of mine because I do that now, despite the lack of letters after my name. I do review protocols for people.

Susan C. Winckler:

You're Principal McNary.

Jennifer McNary:

I'm principal. And I [02:46:00] gave myself that title. I started my company, gave myself a title, and now people hire me to do the thing so I can support all these children. And I think it's really important to start looking at the totality of that because just because you didn't hit what we thought was going to be the thing to hit doesn't mean that it wasn't successful, doesn't mean that it didn't work. Works mean you hit something. It means that maybe Allyson's getting more sleep or that her child is swimming and won't drown in the swimming pool. That means it works. But how could we have known that [02:46:30] swimming was going to be the thing that hit? So, I'd like us to just completely get rid of the primary endpoints, the secondary, stop the hierarchy of endpoints. Thank you. And then the last thing that I want to say, and this came directly from people commenting on my Facebook post about coming here. Okay?

They said, "Please say this." So I'm saying this because I agree with this. Endpoints also have a way of excluding patients. That's near and dear to my heart because six-minute walk test, Austin wasn't [02:47:00] walking. He got excluded. He didn't get drug for three years. That's a problem. So, endpoints have a way of excluding patients, but also they have a way of excluding patients long after studies are over. We talked about payers a minute ago or a few minutes ago, and I just want to report that patients are still not getting access to therapies where the label is broad enough because the study was not done in that disease progression subgroup. And [02:47:30] again, Max gets denied every other month for the therapy that he helped to bring to market. It's his data that this therapy is approved on, but because he stopped walking and they didn't include non-ambulatory patients in the study, payers just want nothing to do with it. So, endpoints have a way of excluding patients up and down the age spectrum. And I think that's something we also need to work on. Okay.

Susan C. Winckler:

So, I know we have some other folks who want to chime in on the endpoint piece.

Dr. Michelle Campbell: [02:48:00]

Yeah. I mean, I feel like I kind of have to.

Susan C. Winckler:

Feel free.

Dr. Michelle Campbell:

And I expect nothing less from Allyson to be provocative. We've known each other long enough and have done enough panels as well. So, I think I'm not going to maybe provide a perspective of how we look about it and think about this.

Susan C. Winckler:

Right, because to the iterative and adapt, I started to get post-regulator shakes.

Dr. Michelle Campbell:

Yeah, right. Right. Right. Right.

Susan C. Winckler:

It's a thing.

Dr. Michelle Campbell:

Or we're stuck and we're sagging. So, I think there's a couple of things and I think you're bringing up some [02:48:30] really great points, like Jenn's last point about the impact in a post-marketing setting. And I would say I think that's an important thing to the broader stakeholder community. And I mean the broadest in that sense because we may encourage as many age ranges in trials and someone's made a different choice in what they choose to bring. But I think when it comes to endpoints, this is my every day. This is literally my every day is trying to think about what do I think I can collect in a rigorous way [02:49:00] that will meet what we need for substantial evidence of effectiveness if we see something positive and that we can describe what we see and that makes sense to our target population that can be done.

So, number one, in a pediatric setting, and even in my adult progressive rare diseases, I know we have a lot of more of the ped side around, but there's adult rare diseases where can we cognitively actually ask these questions to them or can they actually perform [02:49:30] this outcome assessment that really makes sense and be interesting, but if they're not going to be able to follow directions, I'm going to have a lot of missing data and then what am I going to do? So, there's this conversation of do we actually think we can successfully collect this concept that we know is important? If yes, what's the best way to capture this information? So there's a lot of thoughtfulness of that. I will say that sometimes, and Allyson alluded to this, [02:50:00] people like to follow the past recipe books. People are risk-averse. And so, there is this maybe comfort of like, "Well, this was done in another disease and it got to the finish line." Right?

Susan C. Winckler:

Yes.

Dr. Michelle Campbell:

"Yay." But maybe it made sense for that disease and not the other disease of interest. Or maybe that advice was based on thinking from five years ago and maybe our thinking shifted and maybe kind of

should have discussed what we think about this new. Where [02:50:30] I am in the office I'm part of, and I would say this is true in my other offices that have a lot of rare diseases, is that we are open to novel and innovation. We're going to probably ask questions, rightfully so, but we want to have those conversations because we hear this all the time, "Well, the endpoints aren't great." But if I'm not being asked to think about an alternative, and sometimes we will propose an alternative and we get the pushback. "Whoa, we're not sure if that's right or if we can do or whatnot." [02:51:00] But we're reflecting. So, we recognize the endpoint's the piece that is critically important.

And the other piece we have to throw in there is that drug development in rare disease is global. And so, we are not the only health authority. And so, we know the balances is what is my other health authority is going to say and that sometimes that's a very interesting interplay type scenario. But we want to talk [02:51:30] as early as possible, ask us the questions. We know that sometimes folks are afraid to ask us the questions because they're afraid it's going to open Pandora's box and we're going to start digging deeper, but that's the only way we can give the best advice.

Susan C. Winckler:

Right.

Dr. Michelle Campbell:

In terms of what do we look like when we come in? So, I understand the primary, secondary thing. We just approved a drug in Division Neurology One in September where we labeled an exploratory endpoint because we felt that it was informative and critical to put their information out [02:52:00] there. So, there could be a conversation with clinicians and families on making a decision about what this was going to happen. We look at everything. It doesn't matter where it is. Did it fail that statistical testing? Did we allocate alpha? We will look at everything. We truly will look at everything and we'll see what is the story there, right? So, we really do do that.

And so, this does happen. [02:52:30] I know we recently made an approval where actually it was the secondary that was really the important thing. At the same time, this is my voice and I know some of you guys in the room have heard me talk about this is please consider including as much as possible a variety of reporter types in your data collection because that offers us the broadest abilities to capture that actual lived experience and that change. So, if I see a lot of clinician reported [02:53:00] outcomes being asked, I am definitely the person who's going to put back, "Hey, have we thought about capturing something from the caregiver perspective? Can we actually maybe get a performance outcome measure that would make sense?" Because we hear clearly that that clinic visit for that study visit that the child is exhausted at because it's a two-day visit and you've got 17 things you want to do and four MRIs and 10 blood draws and I'm not at home and I'm not comfortable and they didn't sleep on the hotel the night before is not really capturing [02:53:30] what I'm seeing every day at home.

And so, one way to kind of do that is to think about what else can I capture and what are those data capturing opportunities throughout the duration of your trial that maybe you could do some remote data collection as a way to capture this. So, I think we are very much open to having these discussions with sponsors. Please do come and ask us.

Susan C. Winckler:

Yeah.

Dr. Allyson Berent:

But I think it should be with more than just sponsors, right? So, if we put patients at the table, then it's not this big black box of what the sponsor heard [02:54:00] and what they're telling us was said, which is often different, I think. So, if there's a circle and we can all talk, then I think we all understand what we're going for and then we can level the playing field.

Susan C. Winckler:

And from the sponsor perspective, choosing the endpoint is yes, sponsors are risk-averse in this space.

Tom Croce:

Fair.

Susan C. Winckler:

Fair?

Tom Croce:

I think that's come up multiple times.

Susan C. Winckler:

Yeah. And there's no dissent from there. So, we've had a fair number of success stories and then we've heard [02:54:30] some of the challenges. Is there anyone who wants to lean forward and share a lesson learned the hard way, perhaps with the intent of helping others avoid that same pitfall? Anybody want to lean into that and say... Oh, look, there you go. Go ahead. Go ahead, Ashley.

Ashley Valentine:

And I know I have limited time, so I'm going to try to hit on all of these. So, recently sickle cell has had a drug recalled and removed from the market and that was devastating for us in the community because [02:55:00] we already had very few tools and now we have one less and a few others that don't quite work. The lessons that we learned, I think everyone learned a lesson, everyone across the board, regulatory, really the companies learned a lesson. The population learned a lesson, but that for us really came down to clinical trial design. And so again, with the sickle cell population, and I mean you'll find this in other disease states. I mean, I talked to some of my friends that work in women's [02:55:30] health, the stigma or the preconceived notion about a population, unless real energy is invested into undoing that, it feeds into the clinical trial.

So, we were told that during the pandemic and just in general, that people with sickle cell don't enroll in the trials and you fill trials faster ex-US. And so they're taking their trials out of the country. What we saw was that based on trial design in some of these ex-US countries, the trial had to end. It had to be

stopped [02:56:00] because there were deaths that were happening in those trials. And when deaths are happening in children, you have no choice but to close down those trials and to recall the drug. There were no deaths in Europe. There were no deaths in the US. We were widely using this treatment, but because there was such a safety issue happening outside of the US and Europe, the drug is not brought back to the market. And so, the lessons I have said over and over again with the company, and I think it took something like this for them to listen to me, is that [02:56:30] you are not investing in community engagement and you're not investing in patient engagement.

That's why your trials are not filling. The trials are not filling because the patient population's not interested. It's because the trials are not being presented to the patients. It's because the information about a trial is not given to the patient because when you actually talk to someone living with this disease, they'll do anything to mitigate that disease, to live, to feel better. So, that I think is a tough lesson in the community as a whole. I really think that the patients [02:57:00] paid the price for a decision that was made by a company. But what it has done has opened the door for us to have these conversations. And some of the other companies have really started to change how they do their patient preference studies. For example, they'll really come to us from the start to help with patient preference recruitment and some have not.

So, for us, this has been a learning lesson, but it's a really unfortunate tale because that was [02:57:30] a really promising treatment and we still see some companies with that same sentiment that your population's just not interested in trials, we're going to take it abroad. And while people in other countries need these treatments, unless the study design is designed for that region and can mitigate some of those regional issues, then it's not going to translate back here and then we all lose out.

Susan C. Winckler:

Thank you. That was helpful. Yes, go ahead.

Dr. Mona Elmacken:

I just want to respond to some of the comments [02:58:00] that were made. So, a couple of issues. Inclusion, exclusion criteria belong to the sponsor. And that's why, as I said in my first few minutes, we invite patients to come at the end of phase one and phase two studies so they can attend the meetings where we discuss the design for the registrational study. Because if you exclude patients on the studies, they are excluded, you don't have data for this group of patients. We many times ask sponsors [02:58:30] to actually widen, remove those exclusion criteria.

Susan C. Winckler:

Mona, can you put the microphone up a little closer? Little bit.

Dr. Mona Elmacken:

Yeah.

Susan C. Winckler:

There you go.

Dr. Mona Elmacken:

Yeah. And have some stratification criteria on the study so we can include a larger cohort. They usually want to take patients who have less risk, so they make sure that the studies succeed so that they are risk-averse. [02:59:00] So, we are actually with you on that. Regarding the endpoints, I want to respond to the end point comments that was made. So, at least in malignant hematology branch where I personally reviewed studies myself, every study we have patient reported outcomes. However, the data that we receive are so minimal, everything is missing data. Whether it's missing from [02:59:30] the sponsor, whether it's missing from the patients, I don't know, but at the end of the day, we review what we get. Luckily we have like with the CAR T-cell therapies, we have a humongous magnitude of benefits. So, we allow, we approve the products. But if we depended on patient reported outcomes, we wouldn't have done that because we have very, very missing data set and you cannot make decisions.

If a study is 100 patients and you get data for four or five [03:00:00] patients, what are you going to do with it? It would be very selection biased. So, that's some comment about like-

Susan C. Winckler:

Yeah. Some of the complicating factors that we see back to then incorporating-

Dr. Mona Elmacken:

It's one of the biggest factors, the missing data in the patient reported outcomes. So, just a comment on that. And then regarding developing new endpoints, we agree with you. So, there is another issue that, for example, [03:00:30] even in hematologic malignancies, there is the point of minimal residual disease. Should we identify patients with very low tumor burden so we treat them early before they get into... It's not only neurology that's problematic, but then you need to collect this data. So, there needs to be, in my humble opinion, there needs to be some collaboration between sponsors. They should be willing to share the data so we can have a validation of [03:01:00] the endpoint. It's not only the FDA cannot make a decision without having the data and some of the data are there, but [inaudible 03:01:10]-

Susan C. Winckler:

Yeah. Yeah. Courtney, go ahead

Dr. Courtney Lias:

Sure. And I love this discussion about these endpoints. I'm definitely going to take back this information about sort of assessing as you're going, some important things to look at to see where we can incorporate it. But I wanted to raise something that I don't think will be surprising, but is a challenge. And that is that [03:01:30] we have the opportunity to get information from patients in some areas much better than others. So, where patients are more organized, where there is the certain types of conditions that lend themselves to patients sort of having caregivers that are enthusiastic or the patients themselves have a lifelong connection to their disease, we often get a lot more engagement with that community and the [03:02:00] ability to deeply learn these perspectives and apply them more

easily. The rare disease community as a whole is like that in that we do have opportunities to interact with rare disease community like this one and others, but individual conditions within the rare disease community is much harder for us to get at.

Other conditions that are rare and maybe not traditionally thought of in the rare disease communities that do come together are sometimes harder for us [03:02:30] to find those patients.

Susan C. Winckler:

Okay.

Dr. Courtney Lias:

And so, wherever rare disease groups, large or small, can come to places where they can amplify their voice and we can be there, that's really, really helpful. We also have to think hard internally on how can we get that deeper understanding of the perspective and not just hearing from a patient. That's important. I think it's very important to remember that even if you don't have that forum to amplify your voice, even if you don't [03:03:00] have that group that's very large to generate this, give us that voice anyway and we'll do what we can to learn it. But I think it's a challenge when, especially in the rare disease space where you don't have sort of some of that teamwork there, it's harder for us to understand as deeply.

Susan C. Winckler:

Right, right. Tamar, go ahead.

Tamar Thompson:

Okay. I was just going to maybe build upon something that Ashley said and where we at Alexion have learned and course corrected is when you were talking [03:03:30] about the community piece is it really feels like that's patient friction coefficient, that's site friction coefficient. If you interview the patients, if you talk to the patients before you ever begin a clinical study, so it's not just the community engagement piece, but having those conversations earlier and often in that piece really will help to mitigate some of those components. And we've learned that a long time ago. So, now [03:04:00] that piece is embedded in every clinical study that we design. But I just want to bring it back to that point of its criticality. And I'm saying that in the sickle cell community, there's another undertone that we haven't addressed on this stage. And I think it's a very important point too to come back to as well. So, it's not my disease state, but I needed to say it because I'm on the stage, so.

Susan C. Winckler:

Yes, yes. [03:04:30] Well, in thinking here, I think what Dr. Lias just teed up was the idea that some of these communities are perhaps not as organized. They're maturing and sharing their information. In other places you have mature organizations, but they're not being heard. And we need to correct on both of those to be finding the groups that are coming together and then actually [03:05:00] listening and where we know we have communities to listen to what they have to say. Yeah.

Jennifer McNary:

Can I add a lesson learned really quickly?

Susan C. Winckler:

Of course.

Jennifer McNary:

I think it's important. I've had the honor of participating in many ways in advisory committees. We didn't talk a lot about them today, but I think one of the things we've learned is that it's too emotionally charged and too late. And so, what I really wanted to leave this room with was a challenge today to think about how do we get those questions answered [03:05:30] earlier and in a quieter environment where people are not fighting for their lives, right? They're not feeling like they're swimming up against the current. And that's in Duchenne. I've been able to participate in many AdComms for Duchenne, but it's also in other places where patients feel like it's sort of a last ditch effort to vomit everything they know about their disease and everything they know about a drug [03:06:00] that's on a "chopping block." And I think what we've established here through both regulators and sponsors, as well as from patients is that most of us are willing to come to a table and have these discussions and get these questions answered. There are experts in every field, in every place, in every rare disease. Even if you have to dig for them, they exist and we all can help find them. So I think while I love the opportunity to have an open public hearing at an advisory [03:06:30] committee, it's only because that is the last chance you have. And I think if we stop having that be the last chance you have and instead incorporate these conversations, and so my proposal, and it's not my proposal alone because I know there's something brewing about this proposal from other places, is a type patient meeting, a patient meeting where... I didn't coin that, just so everybody knows.

I'm hearing about it. There are [03:07:00] all of these invitations. But to your point, FDA, and by the way, I'm never pointing fingers at FDA for these endpoints, that's everybody, it's inclusive. But to your point, there's not a patient driven request for a meeting other than a listening session or ELP-FDD, which is a broad topic. But if there's a question that needs to be answered or a conversation that needs to be had, we're beholden to sponsors to invite patients to the table. And so that poses a whole other problem.

And so if there's an [03:07:30] opportunity to have these discussions ongoing about changes in what you want, again, coming back to endpoints, if there's a change in what you want and all of a sudden it's more meaningful to you to deal with fatigue than pain, but in 2015 we said pain and now we need to change what we said and go back and say, "Now it's fatigue," we need to have better opportunities to do that. So I think there need to be opportunities before we get to the it's this or nothing moment, because I'm so done with the it's this or [03:08:00] nothing moments.

Susan C. Winckler:

But I think we've been talking about too is, in fact, that's the end, that should be the 25th conversation, not the second, and having it throughout. Okay. I like to always give everybody a final word. And with nine of you, that means we have to start the final word a little early. So here's the tee up. I want to make sure we get your... [03:08:30] You have two options to answer in the final round. You may answer

something that you heard that you want to highlight or something that should have been said but hasn't yet been said. Do we understand the charge? Answer one of those two questions. Now let me tee up your order. Oh, look at me, I put it in alphabetical order. So fire away answering one of those two questions, something you want to highlight, something that hasn't yet better articulated, [03:09:00] and you have one minute and 45 seconds.

Dr. Allyson Berent:

Okay. I'd like to highlight something because I think it's super important. I'm so enthusiastic about this rare disease framework initiative and I think that it answers or it could hopefully answer, based on what I read in the white paper, a lot of what I think patients are advocating for, which is miscommunication by putting patients around the table at every step in a continuum of drug development from before to middle to during and after. [03:09:30] And not only as an advice to the sponsor, but as a requirement to the sponsor that they are there, they're having a conversation and they understand what's being said and they understand what is needed. Then I think it makes everything about the disease a little bit easier for the regulators to hear from the patients and for the sponsor to not have to feel the regulators aren't going to agree.

And that's the big misunderstanding I think that's there, sponsors are afraid they're going to say no, but patient [03:10:00] advocates feel it's necessary, and then we're getting the conversation in a weird triangle. I think bringing us together is hugely important, because patients and families are the ones that are going to say, "What's the benefit? What's the risk? What is that tolerance of risk to benefit? What is meaningful? And do we believe that endpoint is going to measure the meaningfulness?" And not before they enter a trial, but while they're in the trial, because then we can truly understand what is what we're seeing being captured. [03:10:30] And I think a lot of the time the answer's going to be no. And then we can iterate and then we can make sure we design the best phase three clinical trial rather than waiting until after phase three to look back and say, "Uh-oh, we did it wrong." And I think that would be disastrous for rare disease.

Susan C. Winckler:

So to continue to have those conversations-

Dr. Allyson Berent:

Continue. Trusted people at the table, I look forward to helping implement such a thing for rare diseases. Look forward to it.

Susan C. Winckler:

Great. Michelle.

Dr. Michelle Campbell:

[03:11:00] I hope you take home from us, from the three medical product centers, is that we want the patient voice, we use the patient voice, and we know when it's missing and when we need it and we will ask for it. But I want to highlight an area of lessons learned opportunity that was quickly sidebarred

mentioned, but I do think it's important. And why I think it's important, because it does ultimately tie back to the patient voice and the patient lived experience. We celebrate your successes and we cry with the sadness and the failures. We really, [03:11:30] really do.

But we need to learn from both sides. The successes we learn a lot from because we talk about it, but sometimes we don't get to learn from what didn't work. And we need to know that collectively as all stakeholders, and we are one of them, because that can help us be able to provide better advice for future development because we know your number one fear is development will now be stalled in our disease area because of a failure. Data sharing is important in the first step on how [03:12:00] we can learn those lessons. And so we very much encourage data sharing when it can happen and to think about it early, because that is the patient voice that has been collected in that clinical trial. And if we're not sharing that experience, we can't learn to be able to advance and continue to develop better medical products for the future.

Susan C. Winckler:

Thank you. Tom.

Thomas Croce:

I want to go back to Allyson, I think she... And I think the whole panel really outlined why rare disease drug development is different. [03:12:30] And I think that we sometimes take the mindset of maybe we're not doing a 17,000 person trial, but we use the same parameters. And I think we've heard loud and clear that that doesn't work in the rare disease space. I think for me what I'm really excited about this rare disease framework piece is industry's doing a much better job of collecting patient information, bringing patients into the process, FDA is doing a better job, but now how are we bridging the two together? Where does [03:13:00] that synthesis come of that information and how do we use it? How do we make sure it's incorporated from an early, early perspective all the way through? So excited about that. I think great discussion today.

Susan C. Winckler:

Yeah, the bridging helpful. Yes. Mona.

Dr. Mona Elmacken:

I really want to thank the leadership of the FDA for taking this initiative sincerely to have this communication about rare disease and make it transparent, [03:13:30] because what I'm hearing is really there is a gap that needs to be filled, and probably this initiative will give the patients the voice and will give us the opportunity to hear that voice. And I, again, invite patients and sponsors to join forces when they come after completing phase one studies, before designing the registrational studies, every meeting they come to us, we invite both, and I would [03:14:00] love to see both. Thank you.

Susan C. Winckler:

Excellent. So that invitation to, again, continue the conversation.

Dr. Courtney Lias:

As for devices, there are some similarities for devices and drugs and biologics, but there are also a lot of differences. We see a lot of different types of trial designs and we do spend a lot of time trying to think about including currently what are ways that we can help rare diseases, rare populations get the devices that can help them. One of the concepts that [03:14:30] we do use in various areas is data extrapolation. There's guidance on, for example, pediatric extrapolation where maybe you studied in one population and you're justifying why that data can support another. I really encourage the rare disease community to talk with us. We don't have guidance in that area in particular, but are there certain areas where the data in one area could apply in other areas, help us understand where that does exist, help us have the conversation where we could generate it. [03:15:00] So I just want to invite that.

Susan C. Winckler:

Yeah. And I'm struck, I didn't say it earlier, but we'll talk about it with Dr. Tarver, adding CDRH to the Rare Disease Innovation Hub, from the diagnostic odyssey that so many go through, it helps on the diagnostic side to then the devices that might be used therapeutically to the devices that are used in clinical trials. So thank you. Jenn.

Jennifer McNary:

I actually want to highlight the moment talking about the [03:15:30] HD study or patient preference initiative. And I've been lucky enough to have some sidebar conversations with this group and this large group. And I think it's a really good opportunity to be out on the stage talking about we haven't done this yet and we don't know what to do, we don't know exactly what's right and it depends is a whole sentence. And I think this is a really good case study or opportunity to say, "We should be having these conversations in public forums and transparently and all stakeholders," [03:16:00] because I think none of us have enough time to capture data that isn't going to be used or to ask patients to fill out multi-part surveys or to do qualitative research or to spend money or time or resources that nobody has unless it's the right thing to do.

I think that's what I really wanted to highlight is that the best way forward is to have this conversation in open forums together, multiple stakeholders, decide what we're going to do, do it and then use [03:16:30] it. And I think that we've heard that in, Allyson's, Ashley's and also in Emily's conversation this morning. And then the other thing I just wanted to highlight is that this data is valuable and we learned that again today, that it is valuable. And so sponsors should hear that and take a risk once in a while on having some patient experience data as part of their studies, because we just heard it's used, it's incorporated, and we should believe that.

Susan C. Winckler:

Thanks, Jenn. DJ.

DJ Carlino:

I think what [03:17:00] I want to highlight is there's a theme across here and it is access. Patients need access to new therapies, they need access to different things that they do not currently have. And

access does not end at a commercial product. Access, that's sometimes just the start. And so how do we get patients whatever they need covered and so that they can have access once it is approved is something that I don't think that was brought up a ton but I think affects all of us on the [03:17:30] stage.

Susan C. Winckler:

And actually, DJ, we have a minute, talk a bit about some of the things that you're learning in that post-market space and payer component.

DJ Carlino:

From a Novocure perspective, in a medical device, there's something called the valley of death where there is a gap between Medicare coverage. It was approved. So we had an eight-year gap from our first commercial indication to when it was approved by Medicare. And so [03:18:00] this was a treatment for GBM, which is a rare disease, and patients were denied access. Now, Novocure paid for it, but there's something to be said for we want to continue to invest, we want to continue with our R&D. And so having that kind of uphill battle is something we continue to fight, and it's important for everybody. Everybody wants patients to have access. That's the bottom line.

Susan C. Winckler:

And I know that's a key component for all the... [03:18:30] We know the work is not done if we've gotten to the success of a clearance or an approval. Tamar.

Tamar Thompson:

I want to build a little bit on what Jenn said. The data from the patient community is valuable and we've known that for a long time. I opened up and mentioned the STAR and LEAP programs, but with STAR and LEAP, we published, co-published our mechanism and algorithm that we use. It's out there for any of you, and it's been out there since 2023. [03:19:00] After this, I'll get the link in the publication to you, Susan, to share. But the reason I mentioned that is not for a plug for Alexion. It's because the rare disease community is often small and disparate. We have 30 years of lived experience that makes us successful. We built upon two rare diseases that we though were ultra-rare, turns out they're not. And we've leveraged our platform over a 30-year period of time. For those in the community who don't have that [03:19:30] information and those relationships with the patient community and how to start them, there are tools that we can leverage for the framework.

I don't think we're building from scratch and I think transparency is important. So I'm excited that the framework will give the opportunity for those who have something to offer, from the patient community perspective, a baseline to bring into that narrative to help us expand as a community. Because the one thing that I've [03:20:00] learned to love and know about this community is that rare is rare. And I say that coming from other disease states where we're like, "No, don't talk to that person because they work for this company." But in the rare community, we all come together to help each other out no matter what the cause, purpose, because we're all trying to... What is it? All tides, lift the boats, or whatever the analogy is there. And that's what we're doing in this community. And the framework is a great way from the agency to say, "We support that."

And I think we can leverage [03:20:30] what some of the larger companies have learned, and willing to publish in their relationships with patients and demonstrating how valuable that data is to organize it in a structured way for meaningful clinical co-development in the drug development process.

Susan C. Winckler:

Helpful and great to underscore that there are some of those spaces where in fact the information is shared. And so there is an opportunity to have a [03:21:00] different dimension than where we're seeing an absence of sharing information or sharing feedback saying, "Here's what we did with the patient voice and here's the result of it." All right. We started with you, Ashley, and I'll let you get the last word.

Ashley Valentine:

Great. Well, I want to end on a positive note, and I'm a storyteller, so I'm going to refer to the story as the company that just kept saying yes. I will say we have had some really great success stories [03:21:30] coming out of the sickle cell space. And so this one I want to share, top to bottom, a company that's just kept saying yes when it came to figuring out patient preference. And so this company came to us and they were asking us if I wanted to be on an advisory board for a patient preference study. And I said, "You need us to actually design that study for you?" And they said, "Yes." I said, "Okay." And so we said, "Well, to design the study for you, I'm going to put together a bid, a contract, a proposal, because it's going to require us to pull in [03:22:00] many people from the sickle cell disease community, not just me." And they said, "Yes." And so I said, "Well, we're going to have to pay them the same as you pay the doctors." And they said, "Yes."

We said, "Okay." And so we did that. And then what they did was they allowed us to design how we were actually going to do this patient preference study and use community participatory research, which is an investment in itself. But even before we got to the study, I said, "Well, we need to review your survey." And they said, "Yes." And so we did. And so what we were really careful about [03:22:30] was often what you find in patient advocacy is you get... So you skim the top of the advocates that know that patient advocacy exists, the ones that are on email, the ones that come to these meetings. So it was mutual trust. They trusted that we knew how to contact the people that worked at the nail salons that had this disease or that worked at the beauty shops or like my dad who's a construction worker.

And so we were able to find some advocates who reviewed the study. And what we actually found was that there was other complications of the disease that [03:23:00] they had never thought of because they had been talking to providers, not the community. And so they said, "Yes," and they updated the survey. And then we tested the survey and then we were able to field the survey in a way that truly captured patient reported outcomes and patient preference because we worked with several community-based organizations that had established community health workers, we paid all of those community-based organizations, we put them on subcontracts, and then those community health workers proceeded to contact their local constituents, some even translated into other languages. [03:23:30] And that's how we fielded that patient preference study. Then what happened next was we said, "Well, we want to lay a summary." And they said, "Yes." We said, "Okay." And so then we said, "Well, we should publish how we did this framework because this is atypical and you invested in this." And they said, "Yes."

And so we co-authored this paper about this. And even the sections about the impacts of race and stigma and racism in the sickle cell space and how that really slows progression, they let us put that in the paper. And we also discussed questions that they were bringing [03:24:00] to FDA and we looked at the data and we reviewed it. And so far they're the only company to invest that much money, that much effort and that much trust in our ability to be equals in this, even though we're just a patient organization. And what that has done has also opened up the feedback loop. So any type of... I was being sarcastic.

Tamar Thompson:

I know. I know. You saw me.

Susan C. Winckler:

We had the same reaction. You are not just anything.

Ashley Valentine:

I was being sarcastic, but oftentimes that's what we hear. But this company understood [03:24:30] the importance. It was a good business move. It was a good move for the patients. It was a good move for everyone involved. And now even we talk about post-market, we've opened up this communication loop, so they can call on this group and we can call on this group anytime there's a question because they invested in us, there was this mutual trust and we designed this study this way from the very beginning. So that's my tale.

Tamar Thompson:

Can I just respond to two things that I heard? And they're [03:25:00] absolutely true and every sponsor should be doing this is, one, you should treat your patients as you do your KOLs. You should pay them as you do your KOLs. You should not not do that. And I think because I have the inside knowledge of knowing your circumstance a little better, this also is a reflection of leaders who have done this before and successful in other disease states and bringing that [03:25:30] success to the rare market. And so I think there's a trifecta here of what I'm hearing what made those components successful, but pay and treat your patients thought leaders, they are.

Dr. Michelle Campbell:

Well, I'll just say it. The patient is the ultimate KOL.

Tamar Thompson:

Ultimate KOL.

Dr. Michelle Campbell:

They are the ultimate KOL.

Tamar Thompson:

That voice is your currency.

Dr. Michelle Campbell:

This is a very frustrating point for me sometimes when I hear it.

Tamar Thompson:

That is the currency of your future. You have to treat them that way.

Susan C. Winckler:

And I would [03:26:00] say, Ashley, you said there was a story about the company saying yes, it's actually a story about you proposing the solution.

Ashley Valentine:

I had to ask it every time. I said, "Well, you should really let us do that because we're not..." Yeah. So there's also this story here where I just kept asking.

Discussion: CDRH Hub Co-Chair
Michelle Tarver, MD, PhD, Director, CDRH, FDA

Susan C. Winckler:

And absolutely. So please join me in thanking this fabulous panel. You all did an excellent job. I do need you to leave the stage because Dr. Tarver and I are going to choose which two of those chairs we'd [03:26:30] like to use so that we can close out the conversation. It's fine. Dr. Tarver, come on up. I don't know how we follow that actually, so maybe we can't, but what a fun conversation to just [03:27:00] participate in. You and I will take these and have our conversation. Thank you for joining us. I know you've had a busy day with more things in it than you planned.

Dr. Michelle Tarver:

It's always the case.

Susan C. Winckler:

Right? I was just saying that it's been fabulous to have CDRH added to the Rare Disease Innovation Hub. So important [03:27:30] from so many different dimensions. So it means far more what you say about that. So what has it meant to you and the hub and the center to have this integration and adding CDRH into the hub?

Dr. Michelle Tarver:

I think it's a culmination of an important moment. We have been working towards advancing solutions for children, advancing solutions for rare disease, and this is just another step in that direction. We've been part of the hub [03:28:00] as part of the steering committee since its inception, but this next step of being a co-chair shows a collective commitment of the agency to advance solutions for people who are living with rare disease. And that's really important because the way that you know you have a rare disease often starts at the Center for Devices. We give you the diagnosis, the imaging, all the tests, the ultrasounds, all those things that you're interfacing with at the outset is how you enter into the identity of having a rare disease, [03:28:30] and then, along the way, a number of different treatments. And so that's really important. So we need to think about it holistically if we're really going to develop solutions that are going to work for all the patients that need it.

We are delighted to be a part of it. And I think what it reflects, similar to the RISE workshops that they had on the statistics in rare disease, as well as the data sharing, it shows the importance of breaking down siloed development. We have got to look at this more holistically if we're really going to [03:29:00] move the needle. And this is a reflection of that holistic approach.

Susan C. Winckler:

And it reminds me of we opened the day talking about different mechanisms in the patient listening sessions where you have CBER, CDRH and the office of the commissioner listening to patients at the same time. It strikes me that bringing CDRH into this leadership role with the hub helps just extend that even more and the interaction [03:29:30] that's available. So that's great. We've been spending a lot of time today talking about integrating the patient voice into medical product development, and your team has done an excellent job of telling us about some of the unique ways that CDRH does that, but what might you add in... How would you describe that importance to CDRH and how you think about listening and learning from patients?

Dr. Michelle Tarver:

First off, I just want to say it's been an incredible [03:30:00] day listening. I was sitting in the back when I was able to get free from the meetings and listen to the dialogue and how wonderfully balanced the discussion is, highlighting provocative issues, but also providing some solutions, things that have worked. I'm a caregiver for people who live with rare diseases as well as a provider, a uveitis specialist. The people that I see have rare eye conditions. They often have had a long odyssey [03:30:30] of waiting for a diagnosis. And then a lot of the children that I used to treat when I was at Hopkins, we would sit down and have a conversation about the treatment options that are available to them. And I think what's really important about that is we're often talking about the caregiver's perspective, but in some cases the children don't get a voice in the clinical care exchange even when they have a voice to give. And that has been very frustrating to me.

And so I decided as a provider that we were going to sit down and talk, and the parent has [03:31:00] their opinion, but I want to hear what the child wants to do, and then we'll figure out the treatment that meets the needs for both. Because what's really important is you don't get good outcomes with any treatment if the child's not willing to take it and they're not willing to use it and the parent is not willing to deliver it. So that was a lesson learned from me about the importance of listening to that voice and figuring how you get the best outcomes. We've brought that into the work that we do in our center. We've had a very active patient science and engagement program. I had the honor of being the first

director of [03:31:30] it and I've turned over the mantle to Cyndi Grossman, who's done a fantastic job, but it's a continuum of evidence.

We've talked about the patient experience and listening to their story, but it's not enough just to listen to a story. It's important that they have an active, heard, incorporated voice in the work that we do. Patient preference information, I heard that mentioned on the last panel, we put out guidance about that, not just about how it weighs in on our benefit risk decision, but also how it can set performance goals for patients in their studies. [03:32:00] It's really important. It means we're listening. And what's really important is that we capture it in a scientific structured way, because that is the bar we have to make our decisions on. It's written in our statute. So we are here to partner and help collect that information in a way in which that can work. Patient reported outcomes, when we first started, it was hardly part of submissions. Now it's about 50% or more of our submissions have patient reported outcome measures.

People, this is a movement, takes time to make change, but if all of us [03:32:30] are committed to it and are going to create tools that help facilitate that change, we can see a difference. There's one thing that I do want to highlight. We've got a new initiative called the Rare Disease Impact Initiative. I don't know if you've already heard about that today yet.

Susan C. Winckler:

We have not. Please.

Dr. Michelle Tarver:

We just announced it last month and it really is our commitment to ensuring that the rare disease population has resources they need about how to advance medical device development. We've got a website. So if you're interested in what devices have on-label indications [03:33:00] for rare conditions, look at our website. You'd be surprised. It's 2,100 devices, rare indications. A lot of them are diagnostic tests. That's really important because it also can help sponsors know what tests has FDA already evaluated that we know measure those particular conditions and therefore they can use that as opposed to starting from scratch. The other thing is that we want our reviewers to take a more involved and engaged role in suggesting it to sponsors. You know what? Your device, this probably could work in a rare disease population [03:33:30] and plant the seeds because sometimes they just haven't thought about it. And I think we heard on the last panel how important that can be and transformative for many communities.

And then the third thing is that it helps to create transparency and that leads to fostering collaboration and partnership. And that's what we're really excited about is continuing our ongoing work with the rare disease community so that we can help advance some of the diagnostic tests that may be needed as well as some of the therapeutic devices that may be useful in their care.

Susan C. Winckler:

Yeah, [03:34:00] that's great. And it ties into thinking about that helps with that intersection where you have often the diagnostic odyssey to lead to that rare disease, do you know what it is. But then we were talking about even the ability to measure in clinical trials comes too into CDRH regulated devices.

Dr. Michelle Tarver:

Absolutely. Well, measurement's a really interesting thing as we see more and more technologies that are moving into the home to capture data [03:34:30] from patients in a way that they don't have to intentionally engage, but can passively collect information. It may allow for more outcomes and assessments to be delivered that way. And I think that that's one of the opportunities we have here. Our center does a lot with respect to artificial intelligence. A lot of the wearable technologies, they come through our shop. And so that expertise is one of the things we'd like to lend to the communities to help refine outcome assessments so that they can be used [03:35:00] in different types of clinical trial endeavors.

Susan C. Winckler:

Yeah, what extraordinary opportunity. Is there anything you want to do as a final remark as we think about the importance of the patient voice in medical product development?

Dr. Michelle Tarver:

I would say that we are here, we are open, we want to hear, we want to engage, but we don't want to just hear stories. We want active partners that are willing to help us build tools that advance the science, because that is where real change is realized. We all, you [03:35:30] hear from our staff, we're bought in, we want to help, but we need partners to help us deliver the evidence that we need to make a regulatory decision, as well as to push the industry to help think about some of the other ways to capture meaningful endpoints that will be useful for patients and providers in that care journey. So I'm really delighted to see all the people that are in attendance today in person and online. And I know that if we work together, we really can make a true difference.

Susan C. Winckler: [03:36:00]

I don't know that we could have any better words to close the meeting. So we're going to go with that, that if we work together, we can make a difference. I want to thank you all for coming to today's meeting. I'll just do one final note. Our journey of shared learning will be posted online next week with the recording, the slide deck, and the transcript. It'll be at reaganudall.org. Thank you, and everyone have a great rest of your day.