“Informed Consent: More than Just Another Document to Sign” Webinar
November 8, 2024

Shari Targum: Hello! My name is Shari Targum, and I am Deputy Director for the Office of Clinical Policy, Office of the Chief Medical Officer in the Office of the Commissioner at FDA. Thank you for joining us for today's webinar, “Informed Consent: More than Just Another Document to Sign.” When you volunteer to participate in a clinical trial, you serve an important role in advancing scientific knowledge and the development of new treatments. The research community has an ethical responsibility to make sure that you understand why the clinical trial is being done, and the potential risks and benefits of the research. Before agreeing to join a trial, the goal of this webinar is to provide patients, caregivers, trial participants and researchers with an overview of FDA expectations for informed consent.

We have 3 presenters today, who will discuss the purpose of informed consent in FDA-regulated clinical trials, address information included in an informed consent document, and provide insights on how informed consent could be fit for purpose. We also plan to leave time for a few questions about the process of informed consent. Please submit your questions by typing them into the Q&A box, which is located at the bottom of the screen. Please note, we are not able to discuss specific clinical trials or specific medical products. This webinar is being recorded, so the recording will be available at a later date. Our FDA speakers are Ann Meeker O'Connell, Director of the Office of Clinical Policy, and Suzanne Pattee, Regulatory Counsel in the Office of Clinical Policy. We are delighted to have Lana Escamilla here to provide her perspective as someone who has participated in clinical trials. I will now turn to Lana for her remarks. Lana, the floor is yours.

Lana Escamilla: Thank you for that introduction and the opportunity to present. Today, I have participated in 3 clinical trials, and I'm excited to share my experiences. I do want to say, prior to getting into any details that I do believe I have been provided informed consent in each of those trials. Although in hindsight, there are certain questions that I may have asked about some of the information in the documents, or that I think that patients or caregivers, or even some of the study coordinators may want to point out or go into a little deeper for their studies. *Next Slide*.

These are my disclosures.

So, before I start, I just want to give you a little background on Wilson's disease, so you can understand the trials that I participated in. Wilson's disease is a genetic disease, where your body does not get rid of copper. If it is not detected and treated early, serious illness can develop even resulting in death. I was diagnosed at 22 within a matter of a few months, I went from being a relatively healthy college student to extremely ill. I started vomiting several times a day. I had extreme nausea. I was exhausted all the time. I had so much ascites, which is fluid in your stomach that I looked like I was 9 months pregnant, and I just wasn't getting better. So, by the time I was referred to the University of Michigan Medical Center, I was very ill. They did diagnose me with Wilson's disease within a few days, and at that time, we also learned that I had severe cirrhosis fibrosis, and I was placed on the liver transplant. I was so sick at that time that even if I had a transplant, they weren't sure that I would survive that transplant. So, my health continued to decline. And I actually started losing the ability to read and write. I didn't have the energy to even sit in a wheelchair. I was transported by a stretcher sometimes, and so things just weren't looking good, even though they had started me on a standard of care for Wilson's disease. *Next Slide*.

So, my mother was acting as a caretaker because I was so ill, and she did a lot of the coordinating and speaking with the doctors. That's not unusual for ill patients, and when she was talking to the physicians at the University of Michigan, she learned that there was a clinical trial that was going on, and that there was a study drug that was very promising. The study drug was, or the study was, double blind. So, if I qualified, and I decided to join the study, I would either receive the study drug or the drug that they were starting me on at that point in time. So, some of the things that I really wanted to know at that time was, how long is the trial? So, they gave us a lot of information. The trial was 8 weeks. It was in-patient at the hospital at the University of Michigan. It involved all kinds of medications and tests, and I initially declined. I think they gave me so much information that I decided I didn't want to do it, but when I went home, I was so sick I couldn't even feed myself. So, I made the decision to join the clinical trial. I completed the trial. It was the best decision I ever made because I'm still here today. I don't think I would have been without it. And a few months later, I was actually able to go back to college, and I started a maintenance therapy next. *Next Slide*.

So, fast forward about 20 years. I was now a practicing attorney with 3 children, and I learned from my physician that there was a new study that involved taking a study drug once a day. And this drug had similar properties to the drug that I had actually taken 20 years earlier. So, I was very interested at this time. I was in a different place in my life, obviously, than when I was first diagnosed. So, I had different things I really wanted to know. One of them was how long does the study last? What is my time commitment? Will I have to be at the hospital? Will I be at home? You know what types of tests are involved? Are these invasive? Are they going to be painful, such as a liver biopsy? And also would I need a caretaker for any of this? The testing I did qualify, and I did sign up for this trial, and I completed this trial. I actually thought the medicine was great. I was going to continue on it, but that trial was terminated. It was terminated after my participation had actually ended. But there were other participants in the trial at the time. So, I went back to my maintenance therapy and... *Next Slide*.

So, when that trial ended, my physician, Dr. Fred Ascari, who's actually been my doctor for over 20 years, told me that there was some gene therapy trials in progress that I may qualify for. I found this pretty exciting. But, also, I definitely had a lot of questions because gene therapy you know it changes, possibly your genes. So, some of the things that were really important to me were how long does this last? This one was 5 years. What are the tests? You know what are the risks involved? And you know, if there are risks, will I be taken care of? And it was about 30 pages. I went through it several times with a study coordinator. I had phone conversations with my doctor to go over the trial, and what I want to know and what I didn't know, and I ultimately made the decision to do the trial. So, about 4 months after I had the gene therapy infusion, they decided to terminate the trial. I was very surprised, despite being an attorney, who reviews contracts every day. I really did not pay attention to the clause in there that said that the study could terminate at any time, so it never crossed my mind that it would actually end 4 months into what I thought was going to be 5 years of monitoring. And so, I just… this is something I wanted to point out, because it was clearly in the document, but especially with something like this, where my copper has to be monitored. If someone doesn't have the relationship with a physician like I do and does not have health insurance. This could cause problems, in my opinion. And so, I think it's really important for patients and caregivers to be aware that a study could terminate right after you receive that medication, so that they have alternate plans in place. *Next Slide*.

So just to recap what questions that I would ask, or should have asked, if I did not ask them for informed consent. Is it out-patient or in-patient? Is the study a double-blind study? Is everyone receiving treatment? How long will the study last? What are potential adverse effects? How should I expect to feel when I have different drugs? Am I going to feel sick? Do I need to miss work? Will I need a caretaker for these if I am not taken care of by a caretaker on a regular basis? What are my time obligations? And particularly what happens if the study is terminated, and I have an adverse effect because of the study, what happens? Who covers the associated health cost and what protocols are in place to protect my safety and my privacy? *Next Slide*.

So, I just I want to thank everyone for allowing me to share my story. I think it's so important of the clinical trials that are going on, and I appreciate everyone who is trying to advance science and help people with illnesses. Thank you.

Ann Meeker-O’Connell: Right. Thank you so much, Lana, for your insightful presentation. I'll jump in now. I'm Ann Meeker O'Connell. Good afternoon, Good evening, Good morning, Depending on where you've joined us from. So, I serve as the director of the Office of Clinical Policy, and as Shari noted, I am joined by my colleague, Suzanne Pattee. We're going to provide insights from the FDA perspective.

So these are our disclosures.

And, we could probably spend several days here together talking about informed consent, and the various aspects. But, for today we're going to stay at the 60,000 foot level to make sure we have a shared understanding between patients and others who volunteer to participate in trials, and researchers who are involved in the consent process about FDA's expectations for informed consent. We'll also provide insights on how to facilitate a more participant-centered informed consent, including talking about a draft guidance that we issued earlier this year on key information. We'll try to address some of the questions that you provided at registration along the way, as well as highlight resources that may be helpful in addressing questions. But if there are topics that we touch on today that you think a deeper dive into informed consent and the requirements would be helpful, please let us know.

So let's get started. What is informed consent? As I suppose it's a bit of a spoiler alert. It's not just that signature or the document. It is an ongoing dialogue. It's one that involves disclosure of information relevant to research participants in making an informed decision about whether they want to participate or not. And it's a… it is a dialogue that should occur through a process and in an environment that is conducive to discussion.

Our regulations at 21 CFR Part 50 require investigators to obtain consent from individuals prospectively before they participate in a trial, and those regulations have been highly impactful. Informed consent is routinely obtained before people are enrolled in trials. Yet, I think we sometimes lose sight of consent as a process, not just one of the activities associated with enrollment.

And it is a process. It starts from the recruitment materials and extends through the end of a study. It's not something that's one and done, or a checkbox that is completed at the time of enrollment. It also assures there's continued agreement and understanding throughout someone's participation in a trial. So, this means that people have enough time to consider participation. They can ask questions. The consent process can also include assessing how well somebody understood the information presented to them. And this doesn't have to be complex, simple, conversational questions, like, you know, I've just

given you a lot of information. Can you tell me yourself what will happen if you join this study? So, that I know that I've explained this well. That that can also be effective as well as approaches like teach back methods or quizzes. But, the discussion and the actual documentation of consent are only part of the process. During the course of a clinical trial. There may be significant new information that arises that may impact somebody's willingness to continue to participate in a study. That could be an amendment to the protocol. It could be a new finding related to safety. And when that happens, the Institutional Review Board that approved the study needs to determine whether currently enrolled individuals should be provided with that information and given the opportunity to reaffirm their willingness to continue to participate in the study. Oftentimes in the research community that's referred to as reconsent, although you won't find the word reconsent in our regulations.

So now, I want to turn to the 8 basic elements of informed consent that need to be in informed consent under FDA's regulations. Many of these 8 items are self-explanatory, such as an explanation of whom to contact for questions about the research or about research participant rights. And, an explanation of whom to contact for questions about research related injury. I wanted to touch briefly on two, where there's an opportunity for complexity to creep in, and also one where we get questions. So, the first is, when providing an explanation of the purposes of the research, it's very tempting to go to the protocol and pluck out the language that provides the scientific justification for the study. And that can be a challenge. Because that language is often complex. It's scientific. It's technical and consent needs to be in language that's understandable to a non-medical reader. So that's one thing to keep a close eye on. And making sure that the language is plain language that's understandable to potential participants. On risks, reasonably foreseeable risks and discomfort to participants need to be described in the informed consent form. However, it's not necessary to describe every possible risk, especially when doing that would make the form overwhelming, long, and a challenge for participants to read. Information on risks that are more common are more likely to occur, and those that are serious should be described, so that potential participants can understand the nature of the risks.

Speaking of risks, when appropriate, a statement must be included that a particular treatment or procedure may involve currently unforeseeable risks. And this brings us to additional elements of informed consent. These are elements that need to be included when appropriate, depending on the clinical trial. In addition to the one I just mentioned, there are 5 others I wanted to highlight. The third element, which is the cost to participants that are directly related to participation in the clinical trial, and our guidance on informed consent recommends that prospective participants should be informed of both direct and indirect costs of participating. For example, travel to a site or time away from work. Finally, we have, in addition to the additional elements, there is a mandatory verbatim statement included in the informed consent documents for applicable clinical trials. And those are the subset of trials that are required to be entered into the clinicaltrials.gov databank.

In addition to what's in our current regulations, many of you are likely aware that in September of 2022, we published a proposed rule that would, if finalized as proposed, revise the content, the organization, and the presentation of information that's included in informed consent. For example, we propose including the key information provisions from the revised Common Rule, the rule that governs research that is conducted or supported by the Federal government. And those are key information requirements, and an associated draft guidance are topics that Suzanne will cover later in our time together. In this rule, we are also proposing to harmonize with the common rule by adding four elements of informed

consent. One would be a mandatory element that would require informing potential participants about how their information and biospecimens may be used or shared with other researchers for future research. There are three proposed additional elements of informed consent, two that relate to biospecimens, and one that relates to the disclosure of clinically relevant research results. So, if you haven't had an opportunity to review this rule, we include a link to that role here, and I believe these slides will be posted as well.

But thinking about what's in our current regulations, it represents the minimum information that to be provided to individuals as part of informed consent. Consent form also needs to include other information that may be relevant to an individual's decision and their willingness to participate in a trial. But, one of the things that strikes me is that we often forget there's flexibility in how we design consent forms. And so, when we talk about innovative approaches and clinical trials, it's rare that I hear informed consent enter the conversation, and I think that's unfortunate. Christine Lee, who's the Deputy Director for our Office of Minority Health and Health Equity at FDA, has described how we often lose focus, or we often focus only on what's right in front of us. So, for example, in this photo, we focus on the arms and hands and the regulations, the required elements on each of them, and we lose sight of the opportunity to present this information in a manner that is engaging and optimally informative for those receiving it. So, I think, unfortunately informed consent… the current documents tend to be long. They tend to be very complex, and they tend to be legalistic. And so, I think that after decades of empirical research showing how informed consent can be improved, for example, taking full advantage of videos, technology, images. It's time for us to really increase our efforts to implement a truly participant centered approach to informed consent - both a document and the process. And further to engage patients and communities as partners in the design of informed consent. So, sponsors, clinical investigators, institutional review boards, all share responsibility for ensuring that informed consent is adequate. It meets FDA's regulatory requirements, and, I think informed consent should be considered as by those parties, as much an area of innovation as other aspects of trial design and delivery.

And while I say innovation, it's not necessarily about creating something new. In many ways, it's about applying practices that have been helpful in other areas to effectively convey complex information and facilitate understanding. So, the examples you see on the screen aren't to focus on the words per se, but just to show that informed consent doesn't have to look like what we conventionally think of and what I've seen myself in the clinic being handed a thick stack of single spaced pages.

And, there are resources available to help identify approaches that can be leveraged to support potential participants in understanding the research that's being presented to them. So, on the left-hand side of your screen, you'll see some existing resources, and I wanted to highlight three FDA guidances. One that came out in August of 2023 presents FDA's current thinking on informed consent, and that document provides an overview of each of the regulatory requirements. And then has a Q&A section that answers frequently asked questions that we get ranging from what do we do when we have non-English speaking populations that may be enrolled to questions about payments and reimbursement. So, of the other guidances, one is specific to electronic informed consent that was a joint guidance with our colleagues at the Office of Human Research Protections that we put out in 2016. And most recently, last month, we published final guidance on electronic systems, records and signatures in clinical investigations that can help support thinking through Part 11 implications of an electronic informed consent process. There are also, outside of FDA guidance, there are recommendations and resources from the Clinical Trials

Transformation Initiative (CTTI). So, they had an informed consent project in 2016 that includes recommendations on both the process and the document. From a process perspective, the recommendations and resources highlight the need for the individuals involved in consenting participants to be skilled in communicating trial specific information, and to be responsive to the needs of individual research participants. On the documentation side, or the document side, CTTI recommended taking a tiered approach to consent. For example, having a 1-to-2-page summary of the study, followed by a more specific section walking through the regulatory required elements, and then additional information provided in a separate section, including things like the HIPAA disclosure form. So, those are existing resources for ongoing work. I've already mentioned the proposed rule, and Suzanne will talk about the guidance. The draft guidance at the bottom I want to focus on ICH EG (R3). That draft guideline published last year. So, we know that the GCP guidelines are broad. They range from design to conduct, oversight, analysis, and reporting of clinical trials. But despite that broad scope, there are still principles in that document that are related to informed consent. That informed consent needs to be clear. It needs to be concise. It needs to be tailored to the context and understandable.

I mentioned the electronic informed consent guidance from 2016 and wanted to give a few quick notes on it. That final guidance highlights technological advances that could be leveraged to improve informed consent. This guidance really envisions an interactive informed consent that may include diagrams, images, graphics, videos, as well as methods, to assess how well a potential participant understood the information presented to them. And these approaches have a lot of advantages. They can facilitate remote informed consent, allow for hyperlinks to supplemental information and resources that can go into greater detail, if that's desired by a particular participant. And it also gives participants the options of how they want to view information, whether that's listening, watching, or reading, or tailoring a screen to their needs. I don't know how many times you've been on a Zoom or Teams meeting where I'm usually the one saying, can you make the font just a little bit bigger so I can read it. In these systems, that ability to tailor is left in the hands of the potential participant. So that's really beneficial.

Moving on. Another really invaluable resource are patients and communities and really listening to their needs, feedback and interests, and we've had the opportunity to have several recent engagements with patients and communities. For example, last week FDA's Patient Engagement Advisory Committee met for a very engaging discussion of patient-centered informed consent in studies of FDA-regulated medical products, and that advisory committee provided recommendations on the informed consent process and on areas of focus for informed consent that we are actively reviewing.

We've also had the opportunity to have vibrant discussions with FDA's REACH Consortium in September. So, REACH is a research consortium of organizations and institutions responding to health equity focused research needs that was started by our Office of Minority Health and Health Equity in 2023.

And what we heard from REACH centered on three areas. The first and a key component was really about trust. That not, and when we think of consent, we often think about it on a very individual basis. But, this is, adding this community layer and thinking about the communities who may be invited to participate. That there's a need to build trust with community members before approaching them for research, which allows you to then leverage existing trusted relationships with people and organizations, who may serve as trial navigators for their community members, or maybe a valuable resource in providing feedback on the research plan and the informed consent and process. We've already touched on what's in the center, on the value of really thinking creatively, and about consent is more than just a

static document that's in paper and in being creative. That message was really amplified in our discussions with the REACH communities, including designing materials and processes that are flexible and can accommodate a range of different learning styles, literacy levels and cultures. So, lastly, who obtains consent and how they do it was also very important. So, the person who conducts a consent conversation needs to be knowledgeable about the study, and to be able to answer questions about it. But for our REACH members, that alone was necessary, but not sufficient. A key consideration was that that individual also be able to demonstrate caring and compassion, and several communities had found value in training researchers and training staff through things like role play on how to effectively conduct such a consent discussion. So, I think that's it for me. I think I will be leaving you in the very good hands of Suzanne Pattee to talk about the concept of key information. It's another area where knowing what's important to different patient communities matters. So, Suzanne, I am delighted to hand it over to you.

Suzanne Pattee: Thank you, Ann. There I am, and thank you for introducing us so well to so many of the new changes we're looking at FDA for informed consent. In addition to working as a lawyer at the FDA, I also wanted to mention that I, too, am a research participant. I was born with cystic fibrosis, which is a genetic disease and largely impacts the lungs and the digestive system. I've actually participated in clinical trials since I was a teenager. And I'm benefiting today from some amazing new treatments for this disease, which would only have become available because of clinical trials and trial participants. So obviously, this issue is very dear to me.

Today, I'm going to talk to you about this new guidance that we just put out in March, and it just addresses these new provisions that we've just heard about in the draft rule that Ann talked about. So, there are two provisions that we've talked about in this guidance. They are both intended to help people decide whether to join a study. The first provision is that consent forms must begin with key information, which is most likely to help a potential participant understand why someone might or might not want to join a study. Secondly, the second provision we talked about is that informed consent as a whole must be organized, and present information in sufficient detail to help facilitate the person's understanding of why someone may or may not want to join a study. We issued this guidance jointly with the Office for Human Research Protections, which addresses federally funded research through the common rule. These provisions are identical to language in the common rule to help us harmonize with OHRP’s rules as well. The working group worked with agency staff as well, and consulted with patient representatives. Patients and research participants are an important part of this dialogue. We wanted to share these efforts with you today. *Next Slide*.

What might participants expect to see in informed consent in the key information. Key information is the critical information about a study. If the FDA's rule is finalized without changes, then it would require the consent form to begin with key information. This would apply to written forms, to electronic consent as well as the oral consent process. This should explain the study and the reasons why a potential subject may want to join the study. Note that while the regulations use the term “subject,” we acknowledge that many patient communities prefer the term “participants.” Key information also must be concise and focused, and it must be organized and presented in a way that helps someone understand the study. *Next Slide*.

When preparing this key information, the working group reviewed the consent elements from the regulations that Ann just spoke of, and we talked about information beyond the consent elements that also may be appropriate to include. Note that the key information may comprise the entire consent, if it

includes all of the basic elements required by the regulations, such as consent information for simple studies which may fit this model more specifically, more easily. So, I'm going to talk to you about these elements. We've now looked at and considered that they should be included in key information. The first may be just to state that this is key information to help participants better understand the trial. Second, consider stating that participation is voluntary, and it should be based on what is important to participants. Also, they can leave the trial at any time without penalty. Third, consider explaining the purpose of the research to help participants understand what they are being asked to do. *Next Slide*.

The working group recommends that key information address the risks or discomforts and potential benefits. Risk information can be quite complex and lengthy. And, as Ann mentioned, it can take pages if we were to get into all the details. So, for the key information, we suggest only putting in critical points about risks or discomforts in the beginning part. You can include more risk information in the entire consent form. In fact, it may be appropriate to repeat some of the key information about risks in the whole consent, as repetition can help to explain complicated information. The key information also should include the potential benefits. These should be straightforward and balanced and not necessarily overly optimistic. *Next Slide*. Please.

The key information also could include information about the expected duration and procedures, such as the length of the trial, and the number of visits, as well as the procedures that may be done at each visit. Consider including whether any compensation and treatments may be provided, and whether treatments will be covered if someone is injured in the trial. Key information also could include other alternatives that participants may need to consider. We also encourage participants to review the full consent form and speak with researchers, their doctors, and their families and communities as they consider participating. We note that some parties have expressed concern that adding key information will lengthen an already long consent. However, providing concise, clear, key information to help participants understand what they are being asked to do can only improve these complex documents and help participants. *Next Slide*.

Now, key information is not intended to be used in place of the consent process. Rather, it can be used to help make the consent discussion clearer. It is not intended to be a change in the responsibilities for preparing or administering consent. For example, the Institutional Review Board will review the key information along with the entire consent form. It's also not a one size fits all approach. Each study is different. Sponsors should determine what should be considered key for each study. We urge sponsors also to consult with patient groups and communities for each study when developing key information. *Next Slide*.

The second provision in the proposed rule is that the guidance needs to facilitate understanding of the whole consent. If the FDA's rule is finalized as proposed, it would then require the whole consent to provide information in sufficient detail and require the whole consent to be organized to help participants understand why someone may want to join the study. *Next Slide*.

There are many ways to provide key information to help participants understand the study. The working group provided one example using tools and tips to aid understanding. Here on this slide, we show you the example from the draft guidance. We are not focused on the words themselves, since they're tiny, and I know you can't see them. We also just reviewed the content in the previous slides. With this example, we want to explain some of the design tips that we use to organize and display the information

in a way that can aid understanding. Again, this is just one approach. It's not required. You can think of something else, but we think it has some really good merit, so wanted to share it with you today. And we put it in guidance. *Next Slide*.

The working group for this guidance used research conducted by FDA and others regarding how information can be presented to improve the ability of consumers to understand prescription drug labeling. The findings were published in this article shown on this slide. In the study, researchers found that consumers understood the information better when it was provided in a simple format, and when information was grouped together within a defined border. The article called these bubbles. As you will see from the article, the bubble format improves comprehension. *Next Slide*.

Based on the findings in the paper and other resources, such as plain…

Ann Meeker-O’Connell: Think we may have just lost Suzanne. Maybe give her a minute to see if she jumps back on, but if not, I can jump back in and. Joseph, can you confirm you don't see her on anymore? Yeah, exactly. Suzanne. You're back. So.

Suzanne Pattee: My apologies. I'm not sure why it’s done that. I will work on that after the call. So I think we're on Slide 36. So, I think I'm also, let's see. In closing on this slide, these and other design tools can really help participants to better understand the study when figuring out whether they should join. *Next Slide*. Please, Ann.

Again, this is just one approach we recommend. We encourage researchers to consider multiple approaches, be creative and innovative when designing key information and the whole consent. It should be organized better. We can do a better job. Consider using graphics, videos and electronic consent. The guidance also does recommend reaching out to participants and their communities to help identify what information is key to help them understand the study. The guidance suggests two other approaches for key information. Ann mentioned the project for tiers, and in this case, the key information could be provided in the first tier. Or consider preparing a list of questions from participants’ perspectives for key information. And again, consider having research participants and communities review the whole consent material to determine if they really are helpful for participants. Key information is a helpful tool to make consent more participant centric. *Next Slide*.

These provisions may improve more than just consent. The bottom line is that it's critical to have better informed participants. These tools may help presenters to explain information more clearly. Better consent materials can provide useful information for participants to consult later at home. Clinical trial enrollment is often the longest and most challenging part of conducting trials. Having better consent materials and processes may help with trial recruitment and retention. Better consent materials also may help recruit additional communities to address diversity of participants. Consider the needs of participants when preparing consents. If English is a participant's second language, consent should be provided to participants in the language that they can understand. Consider consulting with diverse communities to help improve consent translations and to aid participants to understand and even reach out to additional communities. *Next Slide*.

As Ann mentioned, FDA is developing the final rule, and if we adopt these new consent provisions, then we'll be able to move forward with this draft guidance. When we published it in March, there were 60 days for comments, and maybe 90, and we got quite a few comments that were very supportive of this

flexible approach that we've embraced in the efforts and they supported being more creative to improve understanding. We are also communicating with interested parties on implementation. *Next Slide*.

Informed consent is not just a signature or a document. Documentation is only part of the process. Speak with trial participants throughout the trial to gauge their understanding and continued agreement. Informed consent must begin with key information if the rule is finalized as proposed. It should be organized, clear and concise. Avoid medical and legal jargon. Be innovative, use new technologies like images, videos and electronic consent. And consider using thoughtful design elements, such as the bubbles, to aid understanding of key information and the whole consent. Engage participants and communities to make informed consent participant-centered. You also may want to consider looking for opportunities to improve consent approaches now. And we applaud you for making these efforts. It's hard to write something shorter, but it's really needed to aid understanding.

At this time, we'd like to open the floor for Q & A. Please note that you can send general questions about informed consent and good clinical practice to our mailbox as shown here on this slide. Please note again that we cannot address questions about specific products or specific trials. I'd like to turn it back to you, Shari. Thank you.

Shari Targum: Thank you, Suzanne, and we will now start with the Q&A portion of today's webinar and turn to your questions. We received a lot of great questions, and we'll try to get to as many as possible. So, the first question is for Lana. There were several questions about the length of the consent form. And, Lana, was the length of the consent form ever a deterrent to participation, and was length a problem with understanding?

Lana Escamilla: It for me. It was not a deterrent to participating, but it was you did have to find time to actually review the document because I did look at the last one. It was 34 pages. I think that for some people it could possibly be confusing, but it was not for me.

Shari Targum: A follow up question for the panel. Is there a way to cover all required consent forms in a much shorter and easily understood document?

Ann Meeker-O’Connell: I can jump in on that one, and I think yes. I think you know, a lot of the required elements are not ones that require a lengthy exposition, so conveying that something is voluntary that people can choose to withdraw doesn't take. You know I've seen consent forms that cover that concept in 3 or 4 paragraphs, where it begins to seem redundant. So, I do think there are ways of doing it, you know. I think right now, we're almost a little bit like Dorothy and the Wizard of Oz. We haven't quite yet recognized that we. We have the power to kind of make change. Now, there's nothing stopping sponsors, institutional review boards, and investigators from kind of a looking at, looking critically at their consent forms and kind of making them making improvements now. So, at a minimum, I think I would encourage those parties to consider how the approach is outlined in our guidance could be beneficial.

For example, our 2023 Guidance on informed consent notes that the IRB should ensure that technical and scientific concepts and terms are explained, or common term substituted, so that the anticipated populations that are gonna enroll can understand the information. So, you know, I think in some ways it's upon all of us to look at how we could make it look different. I don't know. Lana or Suzanne, if there's anything?

Oh, we lost Suzanne again. If there's anything you would want to add, Lana, from a patient perspective, or there are kinds of examples of things that you've seen that looked, even if not short, at least kind of easy to read, because that's the other point, I think. Make it as short as possible. But there are some studies where you may need to. Actually, I don't think we should be only looking at kinds of things like word count or page count. It's how clearly was it conveyed. But, I'll stop there and just see if others have anything they want to add.

Lana Escamilla: Yeah. So, I've sat on an advisory board for another clinical trial. And they I believe we're doing some with colors. I think colors are helpful. Some of the bubbles format that you spoke about earlier. It helps break it up when it's just a document with straight print. It's like reading instructions to set up your washer and dryer at your house, and you know a lot of people that are participating in clinical trials really don't have, because of their illness, the comprehension or the ability to even focus on something that long. So I think, breaking it up, the bubbles. Any way you can do that. And if you have your key points, maybe if there's a way to put like appendix, or on the back, or something where they…? If that's what they want to look into, they can see all those risks just to kind of make the key points shorter and upfront.

Ann Meeker-O’Connell: No, and I love that kind of concept of the... Oddly enough, I was at a conference yesterday where somebody brought up the example of color coding, kind of information in the consent form about different study visits, so it made it easier for people to kind of reference things. So, yeah, I think there are a lot of different ways, Suzanne. You've rejoined us. Anything you would add?

Suzanne Pattee: My apologies again. I think the key information could really be landmark here, and I really would hope that we can embrace it. I know it's a challenge, but it's important. And it's also really important to consult with folks, such as Lana, who have the expertise and have been in the trenches with us. So that's all, I would add. Thank you.

Shari Targum: Another question which is related, is it common or considered acceptable to include cartoons or pictures in adult informed consents?

Suzanne Pattee: I can take that. I don't think it's common, but it can be critical. Just because folks are adults... We're much more visual these days, especially with technology. You know, we may look at something for 5 seconds, and we think we understand it. So, we're not as good at details these days. Social media is ruining us for that. So yeah, it's a good idea. Consider it.

Lana Escamilla: If I can jump in really quickly. Going back to when I was first diagnosed and extremely ill, I think that I would have appreciated cartoons, or even being an adult. I really, I agree. It makes it easier to see things, and it breaks up the monotony of just a straight document, and I think it can help people understand.

Shari Targum: Another question is around addressing accessibility within, for example, deaf and blind populations. How can the clinical research community address this? And, I will ask Ann to take that question.

Ann Meeker-O’Connell: Sure I mean, I think if you look at our guidance that we just put out on informed consent, you'll see that we strongly encourage the parties involved in clinical research, particularly the investigators, to ensure that the informed consent documents are ones that are accessible. You know, considering that the population that might be enrolled may include individuals with disabilities. So, we

recommend that investigators provide reasonable modifications, auxiliary aids, and services when necessary to meet the specific needs of the study population. For example, if somebody has visual disabilities, the investigator could use an audio recording of the contents of the informed consent, or a consent form within a large font. Kind of what I was referring to earlier. Again, depending on the degree to which somebody might need it. So, I do think it is something that people should be thinking about as they are a part of trial. Planning is understanding the kind of populations who might be included, and kind of what might be needed to meet their needs.

Shari Targum: The next question is for Lana. Lana, were you informed how your study samples, for example, blood or tissue could be used, stored for future studies and how to withdraw those samples after de-identification?

Lana Escamilla: Yes, that information was in my consent form.

Shari Targum: Another question for Lana. Were there disappointments with the informed consent process that in hindsight could affect your willingness to participate in the future?

Lana Escamilla: I don't think there were necessarily disappointments, but I do think, for instance, I talked about the termination and that happened in my last trial very quickly after I received a gene therapy. And, I mean, had I known that it would be canceled after 14 weeks, I probably would not have done it because one thing that was important to me was the 5-year follow up for safety and protocol. I'm not saying that I regret doing it, but if I had the information at that point, if someone said, “Hey, this might be done tomorrow,” I don't think I would have gone through all the workup and all the additional things I had to do to qualify had I known that. But, I can't say that I'm necessarily like it's hard to explain it. I don't know if that makes sense. But I'm not mad that I did it, but I think sometimes I feel like it's good to not know everything, because you might not do something with the information you have. But, so, I am glad that I did it, but I do think if it had said you might be done in 14 weeks, I would not have signed up.

Shari Targum: The next question is for Ann. What safeguards can the research community have in place to protect the patient to ensure that the patient understands the informed consent material?

Ann Meeker-O’Connell: Yeah, I mean, I know I touched on one of them at the beginning, which you know, was actually something that was talked about during the patient engagement advisory committee meeting that I mentioned that concept of just using simple questions that don't require a lot of preparation. You know.

Generally speaking, more discussion improves understanding, but there are things that people can do. You can incorporate quizzes whether that's kind of as part of the discussion. Some of the electronic informed consent form platforms incorporate quizzes. You can do corrected feedback. Ask a few questions and check for any misunderstandings, but you know there's a wealth of literature that talks about different approaches. So, for example, understanding improved when people were randomized to a pamphlet with illustrations to a bulleted fact sheet with a teach back questions. So, there's a whole wealth of information out there about ways to kind of check understanding. But, I'll go back to, a lot of it is just having that discussion and that engagement.

Shari Targum: Thank you so much, Ann. We are just out of time. Thank you for joining us for today's webinar, which was a joint effort with the FDA Office of Clinical policy and the Patient Engagement Staff in the Office of External Affairs.

We would like to thank our speakers, Ann and Suzanne, and a special thank you to Lana Escamilla for sharing her personal story experiences and comments.

If you have general questions about informed consent, you may send an email to our good clinical practice mailbox gcpquestions@fda.hhs.gov, again, we will not be able to address questions on specific trials or medical products.

This concludes today's webinar. Thank you for joining us.

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