UNITED STATES OF AMERICA

FOOD AND DRUG ADMINISTRATION

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CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

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PATIENT ENGAGEMENT ADVISORY COMMITTEE (PEAC) MEETING

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PATIENT-CENTERED INFORMED CONSENT IN CLINICAL STUDY OF FDA-REGULATED MEDICAL PRODUCTS

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October 30, 2024

10:00 a.m. EST

Via Web Conference

Transcript Produced By:

ACSI Translations

1025 Connecticut Avenue, NW, Suite 1000, Washington, DC 20036

https://acsitranslations.com/

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Patient Engagement Advisory Committee (PEAC) Call to Order

Dr. Roy: I would like to call this meeting of the FDA's Patient Engagement Advisory Committee, PEAC, on October 30, 2024. I'm Dr. Rita Roy, Temporary Voting Chair of this Committee. I'm a general surgeon by training. I spent a career in medical education, and I currently am the CEO of the National Spine Health Foundation. We are the preeminent patient advocacy organization in spinal healthcare. I'd like to speak briefly about the importance of the PEAC Committee, and just remind everybody that this is the only Advisory Committee comprised solely of patients, caregivers, and patient advocates. This Advisory Committee is the most formal and public way that FDA can receive advice from the public on scientific matters. The PEAC has members with expertise in various disease and condition areas, and we have a few additional experts participating with insight on bioethics, public health policy, social science research methods, digital health and machine learning and artificial intelligence ethics, informed consent, including eConsent, mobile health, real world data, applied ethical, legal and social implication research, and much more.

The Committee has made significant impact on FDA's work. For example, the very first meeting ultimately led to FDA issuing a final guidance document on patient engagement in the design and conduct of medical device clinical studies. The PEAC has provided recommendations on FDA's communication efforts related to medical device recalls and cybersecurity risks, and actively contributed to many other efforts, including advice related to patient-generated health data, artificial intelligence and machine learning enabled devices, and augmented reality, virtual reality medical devices. The involvement of patients has increased the work that FDA does, including the

participation in stakeholder meetings, such as those associated with MDUFA negotiations.

It is a real honor for me to be serving as Chair of this Committee, having participated as a Committee member for several years.

I note for the record that the non-voting members constitute a quorum as required by 21 C.F.R., Part 14. I would also like to add that the Committee members participating in today's meeting have received training in FDA device law and regulations.

For today's agenda, the Committee will discuss and provide advice on the topic of patient-centered informed consent in clinical study of FDA-regulated medical products. The individuals who volunteer to participate in clinical research play an integral role in advancing scientific knowledge and supporting the development of potentially life-saving therapies for patients in need. Informed consent is a key element in clinical studies, and can be one of a patient's first interactions with the clinical community. Too often, however, informed consent forms are lengthy and difficult for potential research participants to understand. FDA has worked to improve informed consent over the years, including several recent activities, such as developing a draft guidance in identifying key information in informed consent.

The Committee will provide recommendations on the informed consent process and the areas of focus of the informed consent. The Committee will also provide recommendations on factors to consider when communicating informed consent to clinical study participants, to increase the likelihood of participants understanding the key elements of research.

Now, I'd like to set a few ground rules. If a panelist would like to ask a question, please use the Zoom hand raise function and I will get to your questions as we proceed throughout the day. We want to prevent multiple persons from speaking over each other, since this entire meeting is being transcribed for the official record. Please also remember to remove the hand icon after you have asked your question and provided your comment.

Panel Introductions

Before we begin, I would like to ask our distinguished Committee members and FDA experts identified on the meeting roster and attending virtually to introduce themselves. Committee members, please turn on your video monitors if you have not already done so, and unmute your phone before you speak. I will call your name. Please, state your name, area of expertise, your patient and/or caregiver role as it pertains to PEAC, your profession and professional affiliations. And I'm going to start with Mr. Ian Burkhart.

Mr. Burkhart: Thank you, Dr. Roy. Hi, everyone. My name is Ian Burkhart. I am the President of the North American Spinal Cord Injury Consortium, and my area of expertise is within spinal cord injury research, as well as patient engagement and lived experience research. Thank you.

Dr. Roy: Thank you. Ms. Necie Edwards.

Ms. Edwards: Good morning, everyone. Thank you, Dr. Roy. My name is Necie Edwards and I'm the founder of Fibro Patient Education and Support. And I'm a patient as well as a fibromyalgia warrior. And my specialty is patient advocacy and chronic pain. Thank you.

Dr. Roy: Thank you. Dr. Elizabeth Joniak-Grant.

Dr. Joniak-Grant: Hi. Thank you. I'm Elizabeth Joniak-Grant. I am a Sociologist and I work at the UNC Injury Prevention Research Center. But I'm also a patient experience collaborator there and a Patient Advocate representing chronic migraines, neuralgia, and other types of chronic pain. Thank you.

Dr. Roy: Thank you. Mr. David White.

Mr. White: Hi, thank you. Hello, everyone. My name is David White. I live in Prince George's County, in the great state of Maryland. I'm a proofreader for an international law firm, and I'm a very grateful kidney transplant recipient. My areas of expertise are patient engagement and person-centered care.

Dr. Roy: Thank you. Ms. Teresa Diaz.

Ms. Diaz: Good morning, everyone. My name is Teresa Diaz and I am the Co-Founder of GPAC, which is the Global Patient Advocacy Coalition. And I also facilitate the Breast Implant Health Summit. And I am a Patient Advocate, and that is my specialty.

Dr. Roy: Thank you. Dr. Adam Berger.

Dr. Berger: Hi. My name is Adam Berger. I'm the Director of the Division of Clinical and Healthcare Research Policy at the National Institutes of Health. I oversee all swaths of our clinical research program and anything related to policy, human subject protections. But importantly for this, I oversee our Bioethics Research Program here at the Agency and a number of other aspects that are relevant here, including being a patient myself of a lifelong chronic disease. So, thank you.

Dr. Roy: Thank you. Ms. Megan Doerr.

Ms. Doerr: Hello. Thank you, Dr. Roy. My name is Megan Doerr. I'm the Director of Applied Ethical, Legal and Social Implications Research, ELSI Research, at Sage Bionetworks, a nonprofit open science organization based in Seattle, Washington. My work focuses on integrating community voice into biorepository-enabled research, including through mobile device-enabled research and on informed consent.

Dr. Roy: Thank you. Dr. Camille Nebeker.

Dr. Nebeker: Good morning. My name is Camille Nebeker. I'm a Professor of Public Health and Director of the Research Ethics Program at UC San Diego. And I do and have been doing research for the past decade on digital health and artificial intelligence, and trying to inform how we do informed consent better, as well as how do we return information back to people who are participants in research and thinking through risk assessment and how to mitigate risk. Thank you for having me.

Dr. Roy: Thank you. Dr. Jijo James.

Dr. James: Good morning, Dr. Roy. I'm Jijo James. I am the Non-Voting Industry Representative on this Panel. In my day job, I'm the Chief Medical Officer of Johnson & Johnson MedTech, where my responsibilities span medical safety and patient engagement. Our vision is to ensure a world where those who use our products are free from avoidable harm and realize quantifiable benefit. Thank you.

Dr. Roy: Thank you. Dr. Cynthia Grossman.

Dr. Grossman: Good morning. Thank you. I'm Cyndi Grossman. I am the Division Director for the Division of Patient-Centered Development at the Centers for Devices and Radiological Health at the FDA.

Dr. Roy: Thank you. Dr. George Van Hare.

Dr. Van Hare: Hi, I'm Dr. George Van Hare. I'm a Pediatric Cardiologist and a Medical Officer in the Office of Cardiovascular Devices. I also serve on the IRB for Washington University in Saint Louis, where I have a particular interest in pediatric and family involvement in informed consent processes.

Dr. Roy: Thank you. Ms. Ann Meeker-O'Connell.

Ms. Meeker-O'Connell: Good morning. I'm Ann Meeker-O'Connell, and I serve as the Director of the Office of Clinical Policy and the Office of Chief Medical Officer at FDA.

Dr. Roy: Thank you. Ms. Letise Williams.

Ms. Williams: Good morning. My name is Letise Williams. I am the Designated Federal Official for the Patient Engagement Advisory Committee. Thank you, Dr. Roy.

Welcome from FDA Commissioner

Dr. Roy: Thank you. It is now 10:10 a.m., and we will proceed with welcoming remarks from FDA's Commissioner, Dr. Robert M. Califf. The Commissioner wished he could join us in person today, but had a competing engagement. He provided us with a video as he wanted to share a few words on this important topic.

Dr. Robert Califf was confirmed as the 25th Commissioner of Food and Drugs. He also served in 2016 as the 22nd Commissioner, and immediately prior to that as the

FDA's Deputy Commissioner for Medical Products and Tobacco. He has spent a good portion of his career affiliated with Duke University, where he served as a Professor of Medicine and Vice Chancellor for clinical and translational research, Director of the Duke Translational Medicine Institute, and was the Founding Director of the Duke Clinical Research Institute. He has had a long and distinguished career as a physician, researcher, and leader in the fields of science and medicine. He is a nationally recognized expert in cardiovascular medicine, health outcomes research, health care quality and clinical research, and a leader in the growing field of translational research, which is key to ensuring that advances in science translate into medical care.

AV team, please proceed with Dr. Califf's remarks.

Dr. Califf: I'm pleased to welcome you to today's important meeting of the CDRH Patient Engagement Advisory Committee. I'm sorry I can't be with you in person. Volunteers who participate in clinical studies regulated by the US Food and Drug Administration play an integral role in advancing scientific knowledge about medical products. But that's a point that's often part of a standard rhetoric, but not necessarily fully embraced in the complex clinical research ecosystem. There's a big difference between being a "subject" of research, almost like an inanimate object to be studied and experimented upon, versus being a "participant" in research. And the concept of participation is undergoing an ongoing evolution. I spent a good deal of time throughout my medical career focusing on the importance of strengthening clinical trials to ensure they're more inclusive and designed to produce the best possible evidence to inform decisions, including for our diverse U.S. and global populations.

When we generate high quality evidence, it leads us to the development of medical devices and other products that are most likely to provide benefits that

outweigh the risks that are inherent in any medical intervention. When we don't have high quality evidence in the course of product development and use of the product in practice, we run the risk of harming patients when the product is used in practice. There's also a risk of harm from failing to use the product in situations where the benefits outweigh the risks. In my opinion, including potential participants in the entire process of clinical studies is an important element of generating the most relevant high-quality evidence.

Over the years at the FDA, we've encouraged an increasing focus and reliance on the input of consumers, patients, and their partners in setting priorities, designing, conducting, and disseminating clinical trials. We've learned that shared decision making is preferred when possible, and decision making can only be shared if the relevant information is also shared. Patients' experiences can and should inform and strengthen the entire process, including in ways that help individual patient decision making and formation of policies. For example, enabling the FDA to define meaningful benefits or unreasonable risks for certain new devices more specifically tailored at the individual or population level.

The goal of generating reliable evidence that informs product development and ultimately patient care has several important areas of focus. One, which I already mentioned, involves the intentional effort to improve the availability of trials for those patients who might not otherwise be able to participate; informing our work by supporting our understanding of diverse patient perspectives, preferences, and unmet needs. Additionally, the focus of today's meeting is ensuring that those who become involved in trials are well-informed about the choice to participate or not to participate in a clinical study.

In implementing studies, we all know that investigators should provide information about a planned study to potential participants in a clear, comprehensible way, not just as a matter of respect for the individuals who consider volunteering, but also so that those individuals can make the most informed decisions on whether they wish to volunteer. But multiple studies have shown that all too often this goal is sublimated to lengthy, legalistic consent documents that leave an excellent paper trail.

The FDA is committed to protecting clinical study participants and helping to ensure that the clinical research enterprise welcomes the breadth of participants who receive relevant and accessible information about participating. We published multiple guidance documents providing recommendations on informed consent, and have encouraged sponsors and investigators to leverage innovative products— Innovative approaches to improve participants' understanding of why one might or might not want to participate in research. We hope this will invite broader participation in clinical research to help ensure that clinical studies reflect patient populations who may receive a product if approved, and that these patient populations feel connected to and engaged by the clinical research community.

A few points I'd like to advance. First, research is needed in how to achieve the most effective consent using multiple modalities, including taking advantage of the ability of digital tools to offer potential participants the chance to learn about the study in their own time.

Second, we need to better employ ClinicalTrials.gov, which has a place for recording the consent documents as part of the record of trial conduct. If there was transparency of the broad swath of research consent language and processes, we could learn quickly through research which practices are most effective. Since the vast

majority of interventional clinical trials are included in ClinicalTrials.gov by law, we have a record of all these trials. Let's learn about consent practices at a national scale so we can make it better.

Third, we're not discussing several topics enough, in my view. We don't have enough discussions about the risks of routine clinical care when the right intervention is not known. Discussing uncertainty in clinical practice is unsettling and difficult. We need to figure this out. At the core of much of the discussion of participant interaction is the time allocation of clinicians. As I see the data, potential participants care a lot about the views of the clinicians with whom they interact. But clinicians these days are suffering from high rates of burnout and intense pressure to generate revenue, as they are less independent and more often employees in a system that has been financialized.

I hope that during your discussions, you'll consider that without an engaged clinician, except for protocols that involve relatively healthy participants who participate virtually, the engagement of the participants is difficult. We're making progress, but we still have a way to go. There remains a significant gap in evidence for much of clinical care, and we also have much more work that needs to be done to fulfill the promise of truly participant-centered informed consent. Too often, consent forms remain long, complex, and legalistic, despite FDA guidance to the contrary.

If there's one thing we've learned, it's that we need to listen to participants' input about their experiences and to partner and collaborate with patients, caregivers, and research participants so that we can make meaningful improvements in the informed consent documents and processes. This is why CDRH is having today's Patient Engagement Advisory Committee meeting. Fulfilling the ethical commitment to participants requires high quality informed consent documents and well considered

consent processes that improves participants' understanding of the research they're being asked to consider.

We hope that a strategic focus on informed consent will be another step in helping to ensure that this commitment can consistently be achieved and support our patient-centered medical product development and assessment process. And we look forward to continuing to work with patients, consumers and their relevant allies, and with industry and other communities as we continue to strengthen the important work in this area. Thank you for your engagement in this issue, and I hope you have a productive meeting.

Dr. Roy: I want to thank Dr. Califf for providing those remarks. We appreciate him sharing those insights with us as we consider this a critically important topic. Now, Letise Williams, the Designated Federal Officer for the Patient Engagement Advisory Committee, will make some introductory remarks.

Conflict of Interest Statement

Ms. Williams: Good morning. I will now read FDA's Conflict of Interest Disclosure Statement for the October 30, 2024, Patient Engagement Advisory Committee, particular matter of general applicability.

The Food and Drug Administration, FDA, is convening today's meeting of the Patient Engagement Advisory Committee under the authority of the Federal Advisory Committee Act, FACA, of 1972. With the exception of the industry representative, all members and consultants of the Committee are special Government employees or regular federal employees from other agencies, and are subject to federal conflict of interest laws and regulations.

The following information on the status of this Committee's compliance with federal ethics and conflict of interest laws covered by, but not limited to, those found at 18 U.S.C. 208, are being provided to participants in today's meeting and to the public.

FDA has determined that members and consultants of this Committee are in compliance with federal ethics and conflict of interest laws. Under 18 U.S.C. 208, Congress has authorized FDA to grant waivers to special Government employees and regular federal employees who have financial conflicts when it is determined that the Agency's need for a particular individual service outweighs his or her potential financial conflict of interest.

Related to the discussions of today's meeting, members and consultants of this Committee, who are special Government employees or regular federal employees, have been screened for potential financial conflicts of interest of their own, as well as those imputed to them, including those of their spouses or minor children and, for purposes of 18 U.S.C. 208, their employers. These interests may include investments, consulting, expert witness testimony, contracts, grants, CRADAs, teaching, speaking, writing, patents and royalties, and primary employment.

For today's agenda, the Committee will discuss and make recommendations on patient-centered informed consent in clinical studies of FDA-regulated medical products. The individuals who volunteer to participate in clinical research play an integral role in advancing scientific knowledge and supporting the development of potentially life-saving therapies for patients in need.

Based on the agenda for today's meeting and all financial interests reported by the Committee members and consultants, no conflict-of-interest waivers have been issued in accordance with 18 U.S.C. 208.

For the record, Dr. Rita T. Roy has consented to serve as the Temporary Chairperson for the duration of this meeting. Dr. Jijo James is serving as the industry representative for Communication of Benefit & Risk Information to Patients, and is acting on behalf of all related industry. He is employed by Johnson & Johnson.

For the record, the Agency notes that Dr. Nancy Kass, who is an invited guest speaker with us today, has acknowledged her personal financial interest in the form of communication, consumer discretionary and technology sector funds that contains underlying asset shares and firms that may conduct clinical research for FDA-regulated medical device products that require informed consent. Dr. Kass has acknowledged that as a researcher, she has published extensively on the topic of research ethics, including on the topic of informed consent and her career as an academic faculty whose work is in bioethics and informed consent. She also speaks periodically at professional meetings on the topic of informed consent in general. Dr. Kass has acknowledged her relationship with the National Institutes of Health, NIH, that is in the form of research. She is Chair of the Institutional Review Board, IRB, for the NIH All of Us Research Program, which reviews the informed consent process for this large, publicly funded study and is paid for her services. Lastly, Dr. Kass has acknowledged that her spouse is the principal at Rubix Health, a non-medical device firm which consults with many companies, including medical device companies on matters unrelated to the meeting topic.

For the record, the Agency notes that Dr. Neal Dickert, who is an invited guest speaker with us today, has acknowledged interests with firms that may conduct clinical research for FDA-regulated medical device products that require informed consent in the forms of a grant, consulting, and as a researcher. Dr. Greg Merritt, another invited guest speaker with us today, has reported no interests in relation to today's meeting.

We would like to remind members and consultants that if the discussions involve any other products or firms not already on the agenda for which an FDA participant has a personal or imputed financial interest, the participants need to exclude themselves from such involvement and their exclusion will be noted for the record. FDA encourages all other participants to advise the Committee of any financial relationships they may have with any firms that issue. A copy of the statement will be available for review and included as part of the official transcript. Thank you.

For the duration of the Patient Engagement Advisory Committee meeting on October 30, 2024, Dr. Adam C. Berger has been appointed to serve as a temporary non-voting member. For the record, Dr. Berger serves as a member of the Vaccines and Related Biological Products Advisory Committee in the Center for Biologics Evaluation and Research, CBER. This individual is a regular Government employee who has undergone the customary conflict of interest review and has reviewed the material to be considered at this meeting. This appointment was authorized by Emily Helms Williams, director, Advisory Committee Oversight and Management Staff on October 15, 2024.

Before I turn the meeting back over to Dr. Roy, I'd like to make a few additional general announcements. In order to help the transcriber identify who is speaking, please be sure to identify yourself each and every time that you speak. The press contact for today's meeting is Audra Harrison. For the record, FDA has received two written

comments. Individuals that are confirmed participants for the Virtual Breakout Session have already received Zoom access for this portion of the meeting. Virtual Breakout participants will be instructed by the Temporary Voting Chair to log out of the webcast and log into the Zoom platform to be placed in Virtual Breakout Rooms during the 11:45 a.m. break. Due to limited technology capacity, participants in the Virtual Breakout Scenario Discussion will be limited to 150 participants. Once capacity reaches 150 participants, the Virtual Breakout Session will be closed to additional participants. Please note that the Virtual Breakout Session will not be webcast. The webcast will close at approximately 11:45 a.m. The webcast will remain closed during the lunch break. The webcast will reopen at 12:55 p.m. to allow the general public, as well as those that participated in the Virtual Breakout Session time to rejoin the webcast before we begin the Virtual Breakout Summations at 1:00 p.m. Thank you very much. I will now turn the meeting over to the Temporary Voting Chair, Dr. Roy.

CDRH Opening Remarks

Dr. Roy: Thank you, Ms. Williams. Before I ask the FDA to begin with remarks, I want to provide a brief overview of how today's meeting will run. During the morning, we will have presentations from FDA, Industry and Academia, a Health Care Provider and a Patient followed by Open Committee Discussions. Once the Open Committee Discussions conclude, we will break for approximately 15 minutes. During the break, I ask that those confirmed as participants for the Virtual Breakout Session log into the Zoom link that they were provided, so the Virtual Breakout Session can start promptly at 12:00 p.m. Once the Virtual Breakout Session participants are logged in to Zoom, they will be automatically placed into their assigned Virtual Breakout Rooms. Virtual Breakout Session participants will be asked to participate in the scenario discussion

questions that were provided to them and posted on the FDA website along with the other materials for this meeting. It is very important to note that this portion of the meeting will not be publicly webcast. The Committee members and the webcast will not be available during the Virtual Breakout Discussions.

FDA staff will serve as moderators and notetakers during these discussions and will provide the Virtual Breakout participants with the ground rules for the discussion. FDA staff will not be providing their thoughts or comments during the Virtual Breakout Session. Instead, they will summarize the discussion and report back to the Committee the comments made by the Virtual Breakout participants.

The Virtual Breakout discussions will conclude at 12:30. At 12:30, the public will have a lunch break for 30 minutes. The webcast will reopen for public viewing at 12:55 p.m. Just to be clear, I want to reiterate that I will ask the AV team to close the webcast for public viewing during the 11:45 a.m. break, and the webcast will remain closed through the 12:30 p.m. lunch break. The webcast will reopen for public viewing at 12:55 p.m. Please note that those who participated in the virtual breakout session will no longer have access to the Zoom platform, and will also need to rejoin the webcast to continue viewing the meeting.

When the Committee returns from lunch, we will proceed with the Virtual Breakout Summations. FDA moderators will then summarize the Virtual Breakout discussions for the Committee. Once the Virtual Breakout Summations conclude, we will proceed with the Open Public Hearing. After the open public hearing concludes, we will proceed with the Open Committee Discussions. During this time, the Committee will have an opportunity to discuss the comments from the Virtual Breakout Session as well as the comments shared during the Open Public Hearing. Once the Open

Committee Discussion concludes, we will break for approximately ten minutes. Afterwards, we will return and proceed with Committee discussion of the FDA questions. Following our discussion of these questions, I will give closing remarks and we will adjourn for the day.

It is now 10:31 a.m., and we will proceed with remarks from Dr. Michelle Tarver, Director of the Center for Devices and Radiological Health at the FDA. Dr. Tarver, please begin your remarks now.

Dr. Tarver: Thank you so much, Dr. Roy. Good morning, everyone, and thank you for joining us today for our Patient Engagement Advisory Committee meeting. I'm Michelle Tarver, the director of the Center for Devices and Radiological Health. I want to thank all the members of the Patient Engagement Advisory Committee for serving in this capacity. I also want to thank our CDRH team and others across the Agency for planning this meeting and developing the materials that will help guide our discussion today. We're looking forward to hearing from our speakers, the public, and the audience during our discussion that has focused on patient-centered informed consent in clinical studies of FDA-regulated medical products.

As Dr. Califf mentioned, this is a very important topic to our patients and to all the people involved in conducting studies. That includes study coordinators, healthcare providers, healthcare systems, Institutional Review Boards, and the medical product industries. This meeting provides an opportunity for us to discuss and address one of the most critical issues encountered in the clinical research setting. In fact, clinical research relies on individuals who raise their hand to participate in clinical studies, and it is essential that they understand what they are raising their hands to do. This Advisory

Committee meeting, like our prior ones, seeks the patient perspective with the plan to incorporate those perspectives into regulatory activities.

Allow me to share some of those impacts from prior PEAC meeting recommendations. A few years ago, our PEAC meeting focused on medical device recalls. We heard the importance of communicating early to patients and clearly delineating actionable steps that the person who's using that recalled device should do. We took that recommendation and conducted and published a literature review that examined information on risk communication and about medical products. We reviewed and revised our safety communications based on patient input, and we're continuing to develop ways to deliver recall information earlier to patients.

We've also discussed various different digital health topics, such as artificial intelligence and virtual reality devices, where the patient's perspectives may have great impact in the medical device development and evaluation process. These discussions and the format of the PEAC have helped to pave the way for establishing the Digital Health Advisory Committee. The inaugural meeting will be on November 20 and 21, and will focus on generative artificial intelligence enabled devices. We hope that you will join us and tune in for this exciting event, important milestone, and critical discussion.

Last year, we asked the PEAC for input on our strategic priority efforts related to advancing health equity in medical devices. In particular, the PEAC focused on opportunities to use more medical devices in the home and what would help enable that transition. We heard from the PEAC that while everyone is focusing on the devices, someone needs to pay attention to the home. Not everyone's home is the same, and some of the basic features such as clean water, consistent electricity, internet access, and

movable living spaces may not be a basic feature for many. We heard this feedback and we decided to pay attention to the home. The FDA launched a new initiative, “Home as a Health Care Hub”, to help reimagine the home environment as an integral part of the healthcare system, with the goal of advancing health equity for all people in the United States.

While many care options are currently attempting to use the home as a virtual clinic or a virtual hospital site, very few have considered the structural and critical elements of a home that will be required to absorb this transference of care. Medical devices intended for use in the home tend to be designed to operate in isolation, rather than as part of an integrated, holistic environment. As a result, patients may have to use several disparate medical devices, some never initially intended for use in the home at all, and rather than interact with the medical grade, consumer designed, customizable technologies that seamlessly integrate into an individual person's lifestyle.

CDRH has contracted with the architectural firm HKS, Inc., that intentionally designs innovative buildings with health and equity in mind, to consider the needs of variable models of a home, such as an apartment or a single-family home, or a prefab or motorhome. This initiative includes collaboration with patient groups, health care providers, and the medical device and consumer tech industry to build the home as a healthcare hub. These virtual reality prototypes of homes with the smallest footprint are being informed by people living with diabetes, because it's a condition where we see significant health disparities, and impacts almost every single organ system. The virtual reality prototypes of the home are expected to be completed by the end of this calendar year. We hope that this ideal lab will spur thought, generate ideas, and inspire the development of medical devices and care environments that seamlessly work in the

home that foster engagement, and maximize the quality of life of the people who live there.

It is important that the devices that are developed work for all people for whom they are intended to be used. Clinical studies are often conducted in support of a marketing authorization for a medical device, but they may not always reflect the intended use population. To address inclusive clinical studies and highlight where they might be most impactful, CDRH published a discussion paper entitled "Health Equity for Medical Devices," that describes factors and considerations that may be important for the medical device industry and other relevant parties as they develop medical device clinical studies.

Now, that brings us to today's meeting. Patients or people who are living with health conditions are at the heart of what we do at CDRH, and an informed person is an empowered person. Informed consent is not just a legal requirement, but it is a fundamental ethical principle. Empowering individuals to make decisions about their own health care based on a clear understanding and open communication helps to build trust, foster transparency, and recognizes the unique experiences of perspectives each person brings to the table. An informed consent process and document that uses a patient-centered approach may have broad impacts for many medical product studies. We know that patients who feel heard and respected are more likely to enroll in clinical studies, adhere to study protocols, and remain in the clinical studies, which ultimately leads to improved study conduct and good quality data.

However, we are all here today because the literature suggests that these informed consent documents and processes have been less than ideal, often failing to fully inform participants about the important considerations of participating in the

study. In addition, they may not focus on the information that is most important to the potential participant in that study.

Informed consent is a cornerstone of clinical research and is something so critical it's important that we see a change in how it's conducted. It's important that we get it right. Addressing its current shortcomings is a vital undertaking deserving attention from all interested parties, and today you will hear perspectives from the medical device industry, academia, healthcare providers, patients, and regulators.

I look forward to hearing the discussion and hearing the recommendations for our esteemed PEAC members. And with no further delay, I'm going to turn it back over to our Temporary Chair of the Advisory Committee, Dr. Rita Roy.

Dr. Roy: Thank you, Dr. Tarver. It is now 10:39 a.m., and we will proceed with FDA's presentation. I will remind public observers that this meeting— That while the meeting is open for public observation, public attendees may not participate except at the specific request of the Chair. FDA will have 15 minutes to present. FDA will provide an overview on informed consent and key information by Dr. Jose Pablo Morales, senior medical advisor, Office of Clinical Policy at FDA. You may now begin your presentation.

Informed Consent (IC) & Key Information: An Overview

Dr. Morales: Good morning to all of you. My name is Pablo Morales. I am a senior medical advisor in the FDA Office of Clinical Policy. It is a pleasure and honor to be speaking with you patients, caregivers, and patient advocates today. As a physician, you are the motivation for the work I do. These are my disclosures.

There are four objectives for today. First, define informed consent and informed consent process. Second, describe FDA regulations for informed consent. Third, present FDA guidances on informed consent and electronic informed consent. And fourth, outline the key information guidance.

So, what is informed consent? Informed consent is not just a signature or a document. Obtaining informed consent includes the disclosure of relevant information to research participants that allows for an informed decision by creating an environment that is conducive to the discussions and an ongoing dialog throughout the conduct of the trial. When appropriate, an assessment of the participants' understanding of the research is applicable. A common form of formal assessment of understanding is the teach-back method, in which the person obtaining consent asks the prospective research participant to state back what they understood of what was said. Econsent, or electronic informed consent, platforms will occasionally use embedded questions to ensure understanding.

Regarding the informed consent process, it begins with recruitment materials to the end of the study. It is not once and done. It involves providing a potential participant with relevant information to allow them to make an informed decision. It facilitates understanding; allows for sufficient opportunity to ask questions and consider whether or not to participate; assures no undue influence or coercion; assures participation is voluntary; and assures continued agreement and understanding throughout the duration of participation on the trial.

Documentation of informed consent at the start of the trial is only part of the process. Here I am showing the FDA regulations for informed consent that are divided in three sections. Subpart A includes the general provisions. Subpart B outlines informed consent requirements, and Subpart D describes the additional safeguards for

children. Please note that Part 50 focuses on informed consent only. There are additional protections throughout the FDA regulations in Part 56, which are Institutional Review Boards; Part 312, which is for Investigational New Drugs and Biologics; and Part 812, which is for medical devices.

This slide highlights the general requirement for informed consent under the Code of Federal Regulations, also known as C.F.R. Specifically, they are in 21 C.F.R. Part 50.20. In a nutshell, and paraphrase, the FDA regulations require investigators with limited exceptions to obtain informed consent from individuals before these individuals can participate in clinical investigations of FDA-regulated medical products. Informed consent must be prospective, understandable, and not include exculpatory language. The FDA defines exculpatory language as "language that has the general effect of freeing an individual or an entity from malpractice, negligence, blame, fault, or guilt." Exculpatory language is wording that waives or appears to waive any of the subject's legal rights or the rights of the subject's representative, and the consent form must not include such language. The consent process must also not create undue influence or coercion.

Now that I have outlined the general requirements, I would like to bring your attention to the basic elements of informed consent. The idea is to provide information to participants under Legally Authorized Representative, or LAR, so that they can make an informed decision. The first element is a statement that the study involves research with an explanation of the purpose and the expected duration; description of the procedures and the research intervention; also a reasonable foreseeable risk or discomfort; reasonable expected benefit to the subject or to others; disclosure of appropriate alternatives; confidentiality and that the FDA may inspect the records;

compensation and research-related injuries; point of contact for questions; and that participation is voluntary.

It is the investigator's responsibility to obtain consent, and for the IRB or Institutional Review Board to approve the consent materials that are going to be used in the study.

And when appropriate, depending on the clinical trial, these additional elements need to also be considered. Additional elements, when appropriate, include a statement that the particular treatment or procedure may involve unforeseeable risk to the subjects; circumstances of the study termination; the cost to the subjects; consequences of withdrawal; a statement that significant new findings relating to the subject's willingness to continue participation will be communicated; and an approximate number of subjects in a given study.

Finally, there is a mandatory *verbatim* related to posting the clinical trial in ClinicalTrials.gov. For additional information on informed consent, you may look at our guidance document that is available at the hyperlink shown in this slide. However, we recognize that traditional paper-based informed consent has limitations, especially for sick patients who are often in no condition to read and digest lengthy documents. For patients with poor literacy skills, a paper document is not an effective communication tool.

With these considerations in mind, electronic informed consent, or eConsent has several advantages. It can use a multimedia approach to include embedded videos, graphics, audio, podcasts, and interactive websites to improve understanding. It permits hyperlinks to sites with supplemental information if needed. It can facilitate tests for

understanding. It can be used also to address a variety of sensory impairments, like enlarged fonts, improved contrast, audio recording for visually impaired participants. It also enables expanded use of graphic, audio, and other techniques to improve understanding. And it's easier to update than paper documents.

In addition to aligning with current technological advances, the electronic informed consent process has additional advantages. So, it can be obtained remotely; it offers the opportunity for the study participants to review and sign consent documents in the comfort of their own home; it allows for investigators to interact virtually with the study participants; audiovisual material can show graphically what a study procedures involve, what medications look like, what potential adverse events may look like; and elimination of paper is cost effective, saves time, space, and trees.

So, from the patient's perspective, this could translate into convenience; do not have to go to a research site. Less pressure and anxiety; he can review the consent form and consult with his family or her family members without feeling pressure to sign right away. Participants will likely be more informed, because they can review the consent form at their own leisure, allowing them to make a more informed decision. In addition, supplementing consent forms with electronic technologies could help participants better understand the research. And last but not least, participants can be more engaged, because electronic technology can engage patients more than traditional paper consent documents.

Econsent guidelines recommendations must meet the same requirements as for paper consent. They must include some method to verify the study participant's identity. It must provide an adequate electronic equivalent of a copy of informed

consent. And must be secured with restricted access, and should include methods to ensure participant's confidentiality.

Now that we have touched on informed consent and eConsent, I will share with you to propose provisions about informed consent. We have addressed these provisions in a new joint draft guidance with the Office for Human Research Protections at Health and Human Services, also known as OHRP HHS, and this guidance was prepared by a group of FDA experts from multiple centers along with OHRP. We also consulted with patient representatives for input.

These provisions are both intended to help people decide whether to join a study. The first provision is that consent must begin with the key information, and the second provision is that the whole consent must be organized and presented to help facilitate the participants' understanding of why someone may want to participate in the study. Although this slide is a bit crowded, I'm going to use it as an illustrative example of how to design the key information. Please note that there are many ways to provide information to participants that can help them to understand the study. This example is found at the end of the Key Information Guidance document. We are not focused on the words themselves. Rather, I want to explain the approaches used to organize and display the information to help participants understand the trial.

This example uses a relatively simple trial, and this formatting approach can be used for any study. The Agency recommends in the guidance document that in addition of using plain language, the following tools and aids can be used to improve informed consent. The bubble format with information grouped in distinct chunks, which is easy to understand. The example is limited to a few pages; places the risk and benefit side to side on the first page; uses bullet points to simplify the text. The bulleted information

included in rounded boxes created a small unit of text that is easier to understand. Added hyperlinks to more details in the informed consent form; used simple text where possible; added white spaces and empty spaces around the boxes; and arranged the boxes in two columns on the paper.

Together, these design tools can help make information easier for participants to understand. This approach is intended to provide helpful consideration for how to present key information to prospective participants, to help them understand complicated study information. Starting consent forms with key information will be a requirement when the FDA rule is finalized. Our approach to key information in this guidance is a recommendation, not a requirement.

The guidance also mentions other approaches that can be used, and this guidance suggests that the consent could be organized into tiers with key information in the first tier. This could be followed by the main consent elements in the second tier, and the third tier could include glossaries of key terms or detailed study procedures for the visits.

The example of a key information section in the guidance is just one approach. The Agency encourages creativity and innovation in designing a key information section and in organizing the whole consent form. The use of video, graphics and electronic consent and encourages—The guidance also recommends consulting with patients, groups, and communities to identify what information is key for them to know and understand; and also consider having patients, groups and communities review the consent materials to assess their ability to help participants understand them.

Key information is a very helpful tool in the toolbox of making consent patient-centric, and it should be supported by a fully informed consent form and process that also meet potential participant's needs.

Here are the three guidances I mentioned to you today. The informed consent guidance, the use of electronic informed consent guidance, and the key information guidance. As you can see, the FDA has published guidance documents encouraging approaches that support potential participants in understanding planned research and making an informed decision on whether to participate. However, despite all these efforts, a growing body of literature indicates that informed consent processes and documents have changed very little in practice, despite the FDA recommendations. And informed consent documents often remain long, complex, and legalistic.

We recognize that we as a society are falling short in fulfilling the underlying ethical purpose of informing potential participants about research offered to them, and therefore, more work is needed to fulfill the promise of a truly participant-centered informed consent. FDA is exploring additional ways and methods to optimize and innovate how the research community designs and obtains informed consent in partnership with research participants, researchers and other clinical trials and clinical practice communities. Hence the reason we are all here today and we would like to hear directly from you, patients.

Thank you very much for your attention. In the last slide, I have some additional resources that you can use to get more information about informed consent and the regulation.

Dr. Roy: I would like to thank the FDA representative for his presentation. We will now proceed with an industry perspective presentation by Ms. Allison Anderson, Associate Director of Clinical Trials at Boston Scientific. That will be followed by Dr. Nancy Kass, who is the Phoebe Berman Professor of Bioethics and Public Health, the Berman Institute of Bioethics and the Bloomberg School of Public Health at John Hopkins University, and will give an Academia perspective presentation, followed by a healthcare provider perspective presentation by Dr. Neal Dickert, Associate Professor of the Thomas R. Williams Professor of Medicine, at Emory University School of Medicine. This presentation will be followed by a patient perspective presentation by Dr. Greg Merritt, Founder of Patient is Partner. You each will have 10 minutes to present, and you may now begin your presentations. Thank you.

Industry Perspective

Ms. Anderson: Hi. My name is Allison Anderson. I'm an Associate Director in Clinical Trials at Boston Scientific, and I'm thrilled to be here today to share an industry perspective in relation to informed consent and the informed consent process.

So, I'll briefly start with the elements of informed consent, of which I believe all of you are aware. But from an industry perspective, when we're developing an informed consent, obviously, we want to start the written consent in terms that are easily understandable. And of course, at a minimum, the document should include the reason for conducting the study; what might be unique about this study: is it a new and novel technology? Is it improved features on an established technology or device? Or is it a unique patient population in which a commercially approved device is being used, but perhaps we might be studying if it would be effective for a new and different patient population? The informed consent should cover any unique testing requirements or

follow-up visits, and particularly highlight those that may be unique and outside of standard of care. If a patient is not going to be participating in a study. Importantly, an informed consent must cover risk of study participation, and certainly if there are any risks that differ from standard of care treatment options for the patient's condition. And then finally, it should cover alternative devices or treatments as well.

One thing to keep in mind as sponsors. Often we conduct global clinical trials that may be monitored and governed by regulatory agencies all over the world. And those regulatory agencies may have specific and unique requirements, which have to be included and considered for the conduct of a global study. As well, sponsors have specific elements required in the informed consent, which often results in a lengthy document. Wherever possible, we try to simplify this content using pictures and simple tables, and really with an intention and an effort to make the informed consent document and the process less intimidating to patients. And then finally, while as a sponsor, we have specific requirements that are mandated both by regulatory agencies and general research principles. Each participating study institution may have unique requirements in the informed consent document required by their governing institutions Internal Review Board. And so, while as a sponsor, we provide the Master Informed Consent document, each participating site will likely customize that document and perhaps add additional content as required by their institution, which can make the document even more lengthy.

So, what I really want to focus on today is where do we go from here and what are the future opportunities for patient-centric informed consents and an informed consenting process.

I've had the pleasure of engaging patient advisors who've participated in industry sponsored trials, and these patient advisors have been able to support us with not only designing our trials in a way that's patient-centric, but also helping us identify what supporting materials might be most meaningful for patients as they're considering participating in a clinical trial. As you can see here; some examples. We are often considering printed patient brochures, as well as patient websites and even videos providing an overview of whether the new technology or what it might be like to participate in a trial.

Now, of course, any of these materials that might be used for patient recruitment must be reviewed and approved by a site's Internal Review Board before they can be used with a patient. We are making an effort and see our future as continuing to evolve these supplemental documents and websites and brochures as part of the informed consenting process. The written document will still be there, and there are elements that we must include, as I've already reviewed. But our patient advisors have helped us with developing content that is more patient-centric as well.

In addition to not only the informed consenting process, we've also engaged those patient advisors for how we might consider a patient-centric study design; meaning, how do we limit the burden to a patient for participation and clearly describe if there are any additional requirements that they would need to complete outside of what they might— What they would be expected to do if they weren't participating in the study.

And what I mean by that is ensuring that we're informing the patient if they have to come back to see their doctor for an extra visit, or if they might have to have an extra test. And so that could be clearly covered not only in that informed consent document,

but through perhaps, as you see here in the examples, a video presentation that goes along with the informed consent, or a patient information brochure that they can take away with them and get a better comfort level with what the study might cover.

And then finally, informed consent in most places is still a written process that's completed with hard copy documentation. But we're really living in an online world now. So, we're looking at, you know— Many participating institutions are looking at finding ways to document informed consent electronically. Certainly, during the COVID pandemic, a lot of work was— A lot of work went into how do we appropriately document electronic consents. But overall, we see our future as supplementing that written consent and either allowing it to be done electronically or perhaps, as I said, supplementing it with patient materials to make the overall informed consent process more patient-centric.

So, thank you so much for your time today. Really appreciate the opportunity to share the patient— The industry perspective for how we develop our informed consents and where we see our future headed so that we can continue to evolve and design informed consents and create an informed consenting process that puts the patient at the center of it.

Academia Perspective

Dr. Kass: Hello everyone. My name is Nancy Kass. I'm a Professor at Johns Hopkins University. I'm going to present some data and some thoughts about informed consent. And as the title of the slide says, how is it done currently and what works best.

So, as background, I want to make sure everyone is aware that both the FDA and many, many other federal agencies have had regulations in place for decades governing

most human research. These regulations say several things, but the two most important, and important for today's discussion, are that first, most human research must be reviewed by something called an IRB, an Institutional Review Board, essentially an Ethics Committee that has to look at the research before it's conducted to make sure it's ethically okay. And secondly, the regulations say that most studies will require the voluntary informed consent of participants before enrolling.

The informed consent piece itself has two kinds of requirements in the regulations, again, both at the FDA and in other federal agencies. The first is a requirement for disclosure. There are specific topics, like purpose of the study and risks of the study that must be included in an informed consent disclosure or form. And secondly, documentation. In almost all cases, if a participant— If an individual is willing to participate, willing to enroll, their willingness, their voluntary willingness to join must be documented. This usually is done through a signed consent form.

So, with this regulatory background that we've had for decades, there is what I will call good news and bad news. The good news in my mind is, first of all, that most researchers in the United States know about informed consent requirements. There's a large body of research also that demonstrates what works and what doesn't work to improve understanding. So, we don't have to start at the beginning if our goal is to improve informed consent. And then finally, which I absolutely call good news, is that both the NIH and the FDA believe in informed consent. My sense is that both the NIH and FDA want informed consent to be in place and to be meaningful. And as I'll talk about in a minute, FDA already has some guidance that expressly encourages best practices in informed consent.

The bad news, from my perspective, is that there has not been much uptake of some of the best practices. In other words, as I will go through in a minute, there really are some data that show that certain approaches to consent work or work best or work better. But we have in this context something that is often called an "evidence to practice gap." We know what works, but we're not putting it into practice.

So, here are a few slides about what's going on with consent today. Consent forms have grown longer and longer. There's one study— A published study that showed that the median length of consent forms for lung cancer trials was 21 pages. Another recent study looked at COVID trials and said that the average length of forms was 8333 words, which amounts to 17 or 18 pages. Further, the higher risk the research study, the longer and more complex the consent forms generally were.

Okay, so the whole goal of this disclosure and consent process is to achieve understanding on the part of the people deciding whether or not to join. So, unfortunately, there is a lot of research around what people who enroll do and don't understand, that shows that many participants do not understand why a study is being done, and do not understand its key procedures. In some cases, participants are not clear that they're participating in a research study rather than getting the intervention just as their regular care. And importantly, three different systematic reviews of informed consent, projects that looked at lots of literature at a time, found that one of the most challenging concepts to understand is randomization.

So, empirically, what helps with understanding? In other words, a lot of researchers out there have said, "Okay, maybe we can do consent better." And some of this may seem intuitive. And I guess the good news is research and data demonstrate that a lot of things that intuitively we might think are helpful, really are helpful.

So, studies have shown that there are ways to improve the form, to improve the process. And the bottom line from all this research—I'll show you a little of it—is that simpler and shorter consent forms work better than the longer and complicated ones, and more back and forth dialog helps with understanding compared to just giving someone a form to read and asking them later if they understood.

So, simpler language on a form; using pictures and not just words; having shorter sentences rather than long sentences; shorter forms rather than longer forms. The formatting of the page itself actually makes a big difference in the degree to which people understand. More bullets, rather than just long, dense paragraphs; more white space on the page; having headers that separate out sections; and sometimes framing the header as a question. For example, saying "What will happen if I join the study?" rather than a header that says "Procedures." A summary at the beginning of the consent form, and sometimes even also at the end. In other words, something at the beginning that says "Here are key— We're about to invite you to be part of a research study. Here are key things we want you to know." Then giving all the information and then at the end saying "As a reminder, here are some of the key take-home messages." Those make a difference in improving understanding.

And then similar to that, emphasizing what is more important. One observation about consent forms is that not only are they long, but they essentially treat all of the information and all of the sections as if they are equally important. Whereas in real life, I think most people who join research and most researchers know that while there's a lot of information that has to be conveyed, there are a handful of topics that really are critical to make sure that participants understand.

This is just an example, from one form that has sometimes been thought to be an example. The heading says, “Will my taking part be kept confidential?” And then essentially the researcher would be saying through the bullets, “I will not use your real name in my work. I will lock the information away. This is to keep your information safe so others can't take it.” Again, designed to be simple, straightforward bullets separated out into sections.

Videos have been used increasingly. Of course, it's how so many people learn these days. And they are shown to be helpful. And by the way, don't require the time of busy clinicians the way a traditional consent process does. So, a pre-appointment video, having someone watch a short video about a project before they go into a discussion can help improve understanding. Interactive consent information and maybe little questions for the potential participant on a phone or a tablet can improve. Participants also have said in surveys that they prefer video presentations to reading long forms, and one study found that consent information that was presented through a video resulted in more participants from underrepresented backgrounds, underrepresented in research, joining, including those who were older, black, or had less education; being recruited and also being retained; sticking with the study.

Probably one of the most consistent themes across, again, decades of literature on what improves informed consent is that more discussion improves understanding, and assessing what participants do and don't understand, and then correcting any misunderstandings, are very important interventions for improvement.

So, this second idea is what some people call “corrected feedback.” It either can be a quiz; you ask participants some questions before they can enroll, and if they get something wrong, it can be a pop up that says, “Well, actually, this is— You know, it's

not going to be a one-time visit. It's going to last for a couple of years." Another approach that I think a lot of people like, and it can be informal and not make participants feel like they're being tested, is just a simple conversational set of questions, like saying to someone who's just gone through a consent process, "I have just given you a lot of information. I know sometimes I talk fast. Can you tell me yourself what you think will happen if you join this study? Just so I know whether or not I've explained it well." And that is— And then, of course, if someone stumbles and isn't able to answer it, it's a chance to say, "Sorry, I probably overwhelmed you with information. Let's break it down. Let me go back."

Related to that, it turns out, and there is also research on this, that asking participants to say themselves what they think a study is about reveals better whether or not they understand or what they understand and don't, more than closed ended quizzes do. But anything, to be clear, helps.

So let me just say what I said at the beginning, which is the good news is we have all that evidence. The bad news is we really have a gap in implementation. So, the challenge is we have known for decades that shorter and simpler forms and more discussion improve understanding. And yet at the same time, the forms are getting longer, not shorter, and more complex rather than simpler. Why does that happen and what could help?

So, there have been federal policy updates to try to get us to a better place. The common rule, which regulates so many federal agencies, was revised in 2018 and now requires key information to be presented at the top of all consent forms. In 2016, the FDA published guidance that was about electronic consent, but it included language that said consent overseen by the FDA may include diagrams, videos, narration; may have

methods to help assess understanding, such as optional questions to gauge subject comprehension of key study elements, and highlight areas where the subject might need further explanation and discussion. And then the FDA also this year put out draft guidance on key information. This is to harmonize FDA rules with those of the common rule. Interested parties could consider developing alternate ways to present key information that would facilitate understanding.

So, clearly, the FDA is not only saying, "Let's do key information," but "Think about how you're going to do the information." Consult in advance with patient advocacy groups or prospective subjects; use alternative media such as illustrations, video, electronic tables to meet the goals of improving clarity and increasing prospective subjects' understanding of consent information.

So, this is my last slide. The considerations. There seems to be agreement among participants, regulators, and professionals that current approaches are too long and complex. Consent is broken. And also agreement that simpler approaches work better and people like them more. And in some cases, you retain people better. So why doesn't it happen?

This, I hope, will be part of the discussion. Here are three questions. Does guidance need better dissemination that outlines that simpler approaches are allowable? Do we need requirements rather than guidance? Do we need more advocacy from patients or others to get this in place, or what other ideas may be helpful?

Okay, thanks for your time and I look forward to the discussion.

Health Care Provider Perspective

Dr. Dickert: Thanks very much for the opportunity to talk with you today. I'm Neal Dickert. I am an Associate Professor of Medicine in the Division of Cardiology at Emory University School of Medicine. And I'm going to talk about some of the work that we've been doing within our group and others, partnering with patients to make consent more meaningful. These are my disclosures, none of which are directly related to the work I'm talking about in this presentation, other than research funding.

So, this is sort of where I started. I'm a cardiologist, and I was taking care of a lot of patients in training with acute heart attacks. And patients like this raised a lot of questions for me in terms of how we talk with them about research. This is a patient who's obviously having a heart attack. He's eligible for a clinical trial that might be evaluating a new stent, for example, for treatment of heart attack. And you want to tell him about the trial and ask whether he wants to enroll in it. So imagine, just for a minute, the kinds of reaction that a patient like this might have. And he's unlikely to say, “I'd really like to know more about how my information will be shared. Maybe we can talk a bit about alternatives, and then maybe you could show me some reading materials.” Remember, this is a patient having a heart attack who needs care quickly. This certainly is not what this patient wants. A pile of papers that we often hand people in the context of informed consent for clinical trials. Moreover, a lot of the papers that we hand people tend to read like big red warning signals, giving them indications that maybe it's not such a good idea to sign up for this study.

These limitations are present in acute situations and are really unavoidable. We have a limited time to make decisions. Patients have physical symptoms like pain or shortness of breath. They may have symptoms like fear and stress. These are typically

new and acute conditions for patients, and they often don't have a lot of familiarity with research, which can be very complicated, as you all know. Moreover, we have a lot of patients who lack trust in researchers and institutions, and these conditions can be— These issues can be present in all sorts of medical conditions. I use heart attack because that's really what led me to start thinking about this issue a lot.

So, this got us thinking how do people want to be involved in decisions like this. And so we asked patients who had had heart attacks about different kinds of scenarios. I wouldn't get into the details too much about the specific scenarios, but with various different kinds of studies we were a little bit surprised to find that almost all patients, 75 to 80%, wanted to be asked for consent before making decisions— Before being included in trials like this, in the context of having a heart attack. So this got us thinking, knowing that patients want to be involved, what is it they want out of these conversations, and what do they need out of these conversations to feel respected and make a good decision?

Related to that, we wondered, can partnering with patients help us to make this process better? And then, can we implement, read “get approved”, something that seems more appropriate for the context? So, we did a series of studies funded by the Greenwall Foundation and PCORI that involved interviews with people who had been in acute heart attack and stroke trials. We collaborated— Established and collaborated with nine patients and surrogates to help to really build patient-driven consent processes. And then we implemented those within a couple of trials, one for a bleeding stroke and one for what's called ischemic stroke. And I'll share with you some of what we learned.

Importantly, when we talked with patients, this probably isn't surprising, but it was important that the enrollment process and consent process made them feel like

more than just a number. That individuals interacting with them, especially in acute contexts, acted like professionals. They knew what they were doing, they were there to help them get the help that they needed. People needed to be compassionate and professional. And that they were not pressuring. This is a quote from a patient that reflects a negative interaction where this woman was thinking, “Just go away, please leave me alone.” And then he said, “If you just sign here, we can proceed and I won't bother you anymore.” This is not what we're looking for out of the process.

We also asked people, you know, in part because we thought being handed a form in such an acute time might actually be problematic. So, what do they think about the forms themselves? Interestingly, people were generally not bothered by this. Some people felt like the form actually provided some evidence that the study was legitimate, that it had been approved. Some people thought that the act of signing made them feel like they were formally part of the research. There were people who were a bit aggravated by it, but many people valued or recognized that forms do serve legal functions, and they might be a valuable resource to refer to later. So, we took that and partnered with our patient partners to try to figure out what we could do to make this process better. And these are some of the really key insights that they shared with us and that we incorporated into what we designed.

So first, it's really important that consent forms be realistic and context-appropriate. Any form that's handed to a person needs to be readable in the time frame within which that decision needs to be made. They let us know that first impressions matter. A lot of times, consent forms have things like upfront filler material that is generic information about research generally. They wanted us to start with what matters to them and what's important about the study they're being asked to be involved in.

They gave us really helpful insights about the fact that the negative tone that often predominates within consent forms is not protective. Be honest about reasons that you're doing the study and potential benefits of participation, as well as the fact that you don't know whether it's going to be beneficial, and the presence of potential risks.

They worked with us, and we partnered with investigators to try to minimize or eliminate extraneous information and really focus on the study itself. And our patients really emphasized the notion that boilerplate language that seems to be not connected to the study, they're being asked to consider a risk-compromising trust. We created an information sheet and other materials that could serve as sort of an adjunct. They weren't part of the consent. They contained a much more straightforward and sometimes comprehensive description that people could refer back to, that wasn't designed into the consent form that needed to be reviewed at the time the decision was made. And they emphasized that going back to talk with people afterwards, especially in an acute care context, matters to help people to understand what they're part of and feel respected.

So, we've implemented this within a couple of studies, and it's been really helpful and instructive for us. One is an early surgical evaluation versus conservative management in cases of bleeding stroke. Another was a very large, multicenter study across the U.S. looking at adjunctive treatments to standard therapy in ischemic stroke. And importantly, this was implemented at all of the stroke net sites around the country.

Our experience has been quite positive. Just to share with you concretely what it looked like. In these cases, we had consent forms that really didn't have more than about three pages of key content. We used very straightforward language that was ordered in a way that could follow the conversation, so people could read along while people were actually making a decision. We got rid of generic warning language and what we called

a contextual boilerplate. We used plain language headings, things like “How is this different from what would be done normally?” We had a clear statement of potential benefits as well as uncertainty and reasons for doing the study. And as I mentioned before, a separate information sheet and a structured opportunity for people to learn more about the study later.

I think it's really important to touch on issues related to approval, that may be something people have real concerns about. It is true that this has been very challenging when working with a lot of different IRBs, and there can be local institutional barriers that you confront. It was very productive and really collaborative when we were working with a single IRB where we could have really detailed conversations, and there was nothing more meaningful in all of our conversations than the fact that these changes were driven by patients, rather than being driven by investigators’ perceptions of what mattered.

We are evaluating this now, and we published a couple of these papers already, and there are references linked at the end. We've incorporated a survey of their experiences across all the— Most sites. And in general, we've had a pretty positive impact of feedback from both patients and surrogates, as well as from study teams and human subjects’ protection staff. We need some work to figure out how best to integrate information sheets into consent processes. It's unclear whether this will have an impact on enrollment or representativeness, but we're very encouraged by the fact that study teams and patients seem to have a positive reaction to its use. We've used this in a number of other studies in acute care contexts as well. We're doing it in a trial for pulmonary embolism or blood clots to the lung. We partnered with patient advisors for a sepsis biorepository study at Grady Hospital. And they've had very similar feedback,

and we've structured similar processes for that. And we're establishing a patient advisory panel within our CTSA that can be harnessed for guidance on consent recruitment generally.

So just to wrap up, I think it's really important to design consent processes around what real users want. This is for patients and it needs to be designed around their needs. We have had fabulous collaborations that have really given us great guidance on the process. It's been instructive for us to learn ways in which what many might consider well-intentioned protections are actually not protective. Especially, I'm thinking about really cautious or negative language about benefits in the context of studies. We found that innovations in this space are implementable, especially when collaborating with regulatory bodies and single IRBs, and we still need to learn more about whether this impacts key outcomes or whether people feel respected, whether they feel trust in institutions and investigators, and whether enrollment and representativeness are impacted.

I think it's— I've shared a lot of thoughts that are focused on the acute care context, but all of these insights, I think, are relevant well beyond the acute care context. I appreciate your time, and I'm happy to answer any questions you have.

Patient perspective

Dr. Merritt: Greetings, everyone. My name is Greg Merritt. I'm in Brighton, Michigan and happy to have an opportunity to talk a little today about informed consent and, in particular, thinking about low income and rural patients and the ways in which AI might be helpful. And I'm going to frame most of this through my own story, so you can try to think about it from that perspective as well. So, I raised this as a "questionologist's agenda."

So, this is a word that's largely just made up. Warren Berger was a wonderful author, a journalist who's written a couple of books about this, called "The Book of Beautiful Questions." So, if you have interest, you could go there. But I tend to use this because I care deeply about the idea of how do we remain curious, as patients and curious as people altogether. And so, how I'm going to frame this today is talk a little about my story, of how I got myself into healthcare; I had no real interest. A little of my background, some ways in which AI might be of interest in thinking about informed consent for this population in particular. How trust is going to be really important. And obviously, I couldn't be a questionologist if I don't end with what I hope is some provocative questions for everyone to consider.

So, as I said, I had no real interest in healthcare. If you were to ask me about this, I would have never thought that I'd be giving presentations on informed consent to somebody at the FDA. You know, I was a— Worked in and got a PhD in teaching and learning and ended up working with students in residence halls, building communities there, up until 2012. And in 2012, I had a sudden cardiac arrest and a heart attack. And, you know, woke up one morning, told my lovely bride that I have heartburn. She says you don't get heartburn. And then the next thing, you know, we're driving to Ann Arbor, and about ten minutes away from the emergency room I arrested in the car, and ended up getting to the hospital, did lots of resuscitation in the ER. Thanks to all the folks who do work in that area. Even to one point where the attending asked my wife if she wanted to continue. Maybe some days in the last 12 years she's wondered whether she answered the question correctly. But in the end, what we had is a sudden heart attack, ended up in the cath lab, got two stents, and then used a medical hypothermia, in order to actually

have me wake up and figure out how do I give back to folks who have saved my life and lived this gifted second life.

So, I've been doing a lot of work in healthcare research as a result of that, thinking about ways in which patients can be a really important part of the future of health research. Well, what I will spend time today about is actually my own background in thinking about informed consent, particularly around those in poverty and low-income areas. And, you know, I raised my own background because I think it's a really important question, that's even before informed consent; is how do we even have access to care? Right?

So, you'll see here there's my three-year-old self. And I lived actually in an even smaller town when I turned three. And you begin to see that this is what my little village of 745 looks like today. It's actually a little more populated than it was even when I was there in the late— Early 70s. But if you look down the street, you'll actually see there's a fire station. It's very hard to see in the background, but that's the place where, as a kid, we'd get peanut butter and cheese. And though I didn't actually know it at the time, this was a place where a kid who was in poverty, that's the best we knew about how to get food. And so this is really important as you think about access to care, because as a kid who was rural— My mother at the time actually had a heart attack. And so I start to think, in today's world, how would she have access to any kind of clinical trial? And the answer would have been I don't think she would have. Right? She had three kids that she was trying to somehow feed and care for and tend to, in an environment where she was just trying to make ends meet as best she could.

And so as we think about this, it's both access to care as well as informed consent that we've got to think about. And so why does all this matter? Right? So why

do we care about access to care, informed consent to those who are low income or in poverty. And you'll see a couple of places where annual household incomes below 50,000 are 32% less likely to participate. That's a big number. Clinical trials provide access to all kinds of therapies. And when participation rates of low incomes are— Income individuals aren't there, it just continues to exacerbate this very sad reality between the haves and have nots in the United States.

So, I began to think about, "Okay, there's access to care issues. We've got to figure out how to do that. How do we get folks from these small rural towns to academic medical centers." In my case, it was 30 miles away from Loami to Springfield before you'd even get there. And then when you're in Springfield, you still didn't have this. So, we have to solve that problem. But let's say we do solve that problem. Now we have to think about how would we have informed consent, help those of us in rural low-income areas.

And so, I think about the idea of informed consent can be a place where there truly is personalized informed consent. So, prompts that actually matter, where they're not for people generally, but like me, but they're actually for me. And so it may be that if I think about the people who lived in my town, from the truck drivers to the folks who actually did landscaping and other kinds of things, they would not understand any of this health care stuff, but they certainly might be able to say, "Okay, I'm in this place, I have this condition. I'd like to be a part of a trial. Here's the opportunity for me. But I don't quite understand all the legalese and discussion."

So, maybe the leveraging the current use of AI, and it's going to get better, is to begin to think about how to create a video that will help explain. How to create a podcast, something that they can listen to if they're driving. Some way to create a

picture and visuals that really help you to understand. And that prompt could be not just, again, generic prompts, but saying, “Let me help you to understand how would I create this prompt for you. You know, you're a grandpa who was retired from blah, blah, blah. How— Please, help me understand this, so my eighth-grade granddaughter might even understand this,” so he can help them to see how it's really informed for them.

And so, here's some— A few questions to provoke maybe a movement about how this might happen. So, how might we invite— Innovate to close the gap between those really authentic informed consent for people who are not a part of academic medical centers? How do we close that gap? What if, for example, we invited low-income patients to help solve this problem together with researchers? How would we do that? And how might we find truly trusted community members to begin explaining? For those who actually do participate, are consented, do find their way in trials? How might we leverage that where they know— What they know are churches and bars and post office and fire stations, and schools and places where if that trusted member of the community were able to talk about this and show the ways in which they were informed about what mattered to them, and could choose to not do it further, but it could trust more. And that requires to find people in these small towns and figure out how do we scale this from my town of Loami of 745 to the nations version of these rural towns, some of which have— You know, when I say 30 miles away, that might be a gift to some towns, particularly out west.

So that's my opportunity to really think about how we might do informed consent. And I'd love to have a conversation with everyone about how do we begin to move this new technology in a way that actually fits those of us who come from backgrounds that are low income, that have spent time in poverty, that understand what

it's like to do this. Because if we don't do this well, we're always going to have this gap between those who participate in these trials and those who actually are left out of being a part of something that can fundamentally change their lives.

I'm happy to discuss more. You can see my contact information here. I appreciate your time and attention and look forward to the conversation.

Open Committee Discussion

Dr. Roy: I would like to thank all of the FDA members for their presentations, and I would like to thank Ms. Anderson, Drs. Kass, Dickert and Merritt as well for their presentations.

Now we will have Open Committee Discussion and clarifying questions from the Committee. As a reminder, although this portion is open to public observers, public attendees may not participate except at the specific request of the Committee's Chair. Additionally, we request that all persons who are asked to speak, identify themselves each time, and this will help us with transcription. I'd like to note also, we are running just a few minutes behind. We will end this session at 11:45. So, we've got just about 12 minutes here. So, let's keep our questions succinct and answers as well, so that everyone who's got a comment or question has an opportunity to speak. So, let us begin.

And does anyone on the Committee have any clarifying questions for Dr. Morales, Ms. Anderson, Dr. Kass, Dr. Dickert or Dr. Merritt? Mr. White.

Mr. White: This is David White. Thank you, Dr. Roy. I have a clarifying question for Dr. Morales. At the early part of your remarks, you discussed how informed consent materials should not include exculpatory language. I was wondering if you could explain that a little bit.

Dr. Morales: Yeah. Thank you. Can you hear me, Mr. White?

Mr. White: Loud and clear.

Dr. Morales: Yeah. So basically, exculpatory language— And that's what I kind of thought that someone may ask me the question, and that's what I went ahead and tried to put the definition. And I think, in a nutshell, if I have to paraphrase this, I will say exculpatory language will be a document with language that implies that as a patient, by signing up the informed consent to participation, you're giving away your rights, your privilege, and your autonomy. Right? So, we often see this blended as a legalistic or cause-related that say, "We're not going to take care of this," so you're going to get the right away. But then the question will be for the patient, "Okay, then who is going to take care of that?" Right? Because someone will have to take care of that. So, we want to make sure that the informed consent forms do not have such language that appears that participants are giving away their rights. Does that clarify your question?

Mr. White: Yes, it does. Thank you.

Dr. Roy: Thank you, Mr. White and Dr. Morales. Next question will be from Dr. Joniak-Grant.

Dr. Joniak-Grant: Hi. Thank you. Elizabeth Joniak-Grant. This question is for Nancy Kass. I was curious if you could speak a little to— Concerns about how data is stored. You know, as more and more stuff is kind of stored on systems, what would be from your perspective best practices in terms of making patients aware of risks with data storage, what information are patients looking for, etc.?

Dr. Kass: Yeah. Thanks for the question. This is Nancy Kass. I actually think that is the kind of conversation that would be great to get patient's perspective on. And I don't mean to be hunting on the question, I'm going to say a couple general comments quickly. The first is— My sense—Dr. Dickert may have input on this also from his research—is that that may not be the first priority of people who are joining a clinical trial related to their health care, but it is something that is important to disclose. I often think that general kinds of themes may be even more important than specific ones, by which I mean, letting people know that other people may have access, but they are also subject to rules, or what kinds of groups would have access for what kinds of purposes. My last comment is that I do think that it— Something that we rarely do in research is compare what happens in research to what happens in clinical care. And I think that in our disclosing to participants what will happen with their data in research, it might be helpful to give as context the really stunning degree of sharing that happens in clinical care that I think we don't talk about. Just to put in context, whether the sharing in research seems similar or different.

Dr. Joniak-Grant: Thank you.

Dr. Roy: Thank you. Next question from Ms. Edwards.

Ms. Edwards: Hi. I have two questions. One is for Ms. Kass, and then the other question —I'll be real brief— is for Greg Merritt. So, first I'd like to start with Mr. Merritt. So, Mr. Merritt, I believe you were the one that indicated about how helpful AI can be with the informed consent process and helping to educate patients. My question for you is, although there are many benefits to this, what have you considered doing to make certain that these AI systems are properly trained or is not eliminating certain groups of patients to take those experiences into account? And then my second question

is for Nancy Kass. You mentioned about— You mentioned blacks and other people, low education, may not understand about the clinical trial process. I'd like to know more about what were the demographics of those patients. How many were African American that you surveyed? Because there are many people who don't understand clinical trials, the consent process. I feel a lot of that has to do with how it's was communicated. Those are my questions. Thank you.

Dr. Merritt: Hi, this is Greg Merritt. I'll start by saying I certainly would not describe myself as an AI expert. That's not sort of what I find myself here. What I would say more generically is that I think it's part of the process that we're really new into this. And so, what I care about in terms of the use of AI is to really think about ways to personalize something. So, one of the challenges I have with lots of trials is that we don't do what I would describe as careful and kind and compassionate trials. That means we treat you not people “like you,” but actually “you”, which— So the opportunity, I think, with AI is to actually allow you to— For you to craft what is the prompts that you want to utilize for you to understand something that might be more challenging for you to understand. And that's particularly true in places like my hometown as I think about that group. So, in large measure, I think lots of what you're describing is really important. It will be critical that the future of AI does not actually reinforce issues of discrimination. But I think we're in really early days, and I think if we don't start thinking about this now, we'll find ourselves on the wrong end of this. So, I think this is why it's so important to me.

Dr. Roy: Thank you.

Dr. Kass: For the question addressed to me— This is Nancy Kass. First, let me clarify that I was not presenting my research. This was not a survey that I did. So, I'd

like to make that very clear. In going through the literature, and I'm happy to send the particular paper to the Committee afterwards, that that particular bullet that you're referring to was from— There was a researcher who found that in doing some of these simpler procedures, they simply reported in their study that people from a few different backgrounds were more likely to join and also to be retained. And this did include what they described in the study as Black people and people who were older. But I'm happy to send that study and paper to the FDA organizers so that they can distribute it to the Committee.

Ms. Edwards: Thank you.

Dr. Roy: Thank you, Dr. Kass. We have one more question. If I could remind everyone, please state your name when you're asking a question and responding just so transcribers get that down. So, next question. Dr. Nebeker?

Dr. Nebeker: Thank you. Camille Nebeker, UC San Diego. My question is for Dr. Kass or Dr. Dickert. I'm thinking about the recommendations and what you've learned from the literature, what you've done in your research. We know what we need to do to make consent better. And when I think about the ecosystem, we're not incentivized to make consent better. That's why it's not happening for the most part. So, how would sponsors of research, whether it be narrow clinical trials where we know what questions are being answered, or for biorepositories or data repositories like the All of Us Research Program, what could be done differently? What could sponsors do to affect change in this area?

Dr. Kass: Neil, do you want to start? I've talked a lot.

Dr. Dickert: So, I'm happy to think about it. I think it's exactly right. There's a lot of incentives— Actually, I would say there's incentives not to do this right in terms of getting through IRBs, all of this, you know, this process. I think sponsors encouraging

mechanisms for generating patient stakeholder input when you're putting together recruitment materials and consent forms and budgeting for that, it doesn't have to be super expensive, but expecting people to do that and encouraging them to do that is really important. I think, in the context of the clinical trial space, sponsors willingness to listen to feedback like that and say, "Look, we think this is important to do." And putting through consent materials and recruitment materials that may look different from what their sort of template has in the past is really important. And listening to language, listening to suggestions like the question before about privacy protections.

We did a stakeholder group recently where they told us, "Look, what we really want to know is you're protecting our health information the same way we would in the clinical context, the same kinds of things that would normally be done." The way that language typically gets written looks like there's some sort of special privacy risk, special kinds of things that are going on in the context of research. And what they really want to know is this is a lot like what's going on in other contexts. So, I think really learning about what the meaning is of the information we're communicating and providing the infrastructure people need to be able to do this and do this well. I think the needle can get shifted over time. It's not going to be all at once.

Dr. Roy: Thank you. I will be calling on folks to ask questions and/or respond. We've got just one more minute left on our timer here. And I do see one hand up. Adam Berger, if you've got a quick question and a quick response, please.

Dr. Berger: Not sure it's quick, so I'll go ahead and pose it and you can determine if it needs to be kicked to later on. It's really a question to all of our speakers here. And thank you all very much for presenting really clear considerations for us to be thinking about for improving the consent process. Often we're thinking about this from the standpoint of what's happening within the trial itself from the beginning to the end, but

there's an aspect that's somewhat missing here and at the risk of potentially lengthening clinical informed consents. I'd like to get your thoughts on considerations we should be thinking about for including information about what happens after the study. And I think for CDRH in particular, I think about this from implantable devices that might be staying inside of a patient after the study, after the study ends. That research participant is going to have to think about this before they actually start the study. These are things that are often not necessarily included in consents, though. So, I'd love to hear your thoughts on informed consent and whether there's a need to address the post-trial period and what might be appropriate, and what might be the best way to do this. So again, sorry, I don't think it's a one-minute response, but thank you.

Dr. Roy: Thank you. We will take brief responses here. We can go over just a little bit here. And if you could lower your hand when you're done speaking, and if someone would like to raise their hand to respond, I will call on you. Thank you, Dr. Kass.

Dr. Kass: This is Nancy Kass. My brief response is that may be part of what patients consider to be key information. And that may be true both for drugs and devices, but obviously for devices, if they're in you, that may be key information. So, I think getting sense from patients and participants, what they consider to be key will help to drive what's in that short key information section.

Dr. Roy: Thank you, Dr. Kass. Dr. Dickert?

Dr. Dickert: So, typically I agree with what Nancy said, but I think focusing on what's important in the moment and what's important on a longitudinal basis. Just to give you an example, I did mention some things that might be really relevant to the upfront decision making. In contrast, there are a lot of follow-up kinds of information that might not be relevant for the initial information, but it's really important to provide people on a

more longitudinal basis. So, I think figuring out in a really contextual way what people want to know up front and what people want to know over time, and how to design materials that align with that for the context that's being examined is really important.

Dr. Roy: Thank you. And Mr. Merritt?

Mr. Merritt: Greg Merritt. Again, what I'll say about this sort of generally is more about the notion of what it means that we lose when we think about informed consent over a period of time. Too often, in my view, we lose a community of patients who actually have been part of a trial, not just sort of the device, and we don't leverage the notion of saying, “Would you like to continue to be connected to one another?” As human beings, we often want to be a part of communities, and we are when we join a trial. But typically, money runs out and we just sort of say to the group at the end, “Well, thank you for your participation. Maybe we'll send you a certificate.” But overall, we miss opportunities for maybe 5%, 10% of those people who say, “I want to stay connected to one another post-trial.” And I think there's opportunities to think about that in informed consent at the beginning.

Dr. Roy: Thank you. I have one comment that I'd like to make to the group. And as a patient advocate, it is so important that UX design on the forms that happen are carefully thought through. And it's been said by several here that there has to be appropriate budget allocated in the design and development of the informed consent. And stating this to everybody and also to industry representatives, that's often sort of a thing that's considered easily chopped off the budget, “Let's just chop that off.” But thanks to generative technologies, we really can make multimedia assets that are easier for patients to interact with. So, I just wanted to share my thoughts and comments there from my perspective as a patient advocate.

With that said, it is now 11:48. We will break for approximately 15 minutes. During this time, those that are confirmed participants for the Virtual Breakout Session will need to log out of the webcast and log in to the Zoom link they were provided so the Virtual Breakout Session can start promptly at 12 noon. During the Virtual Breakout Session, I invite those confirmed participants of the Virtual Breakout Session to participate in discussions that are focused on the scenario questions that were previously provided to them, as well as included with the background materials posted on FDA's website for the meeting. FDA moderators will provide Breakout participants with additional instructions for the Breakout Sessions once they are logged into their Virtual Breakout Rooms.

As a reminder, this part of the meeting will not be webcast. The Committee members will not be present or participating. The Committee members, those audience members that are viewing via webcast who are not participating in the Virtual Breakout Session, and those who participated in the Virtual Breakout Session will all rejoin the webcast at 12:55, five minutes before the meeting reconvenes at the conclusion of lunch. Committee members should return to the Zoom platform, and those that are viewing the webcast will need to rejoin the webcast at 12:55 to continue viewing the rest of the meeting. The meeting will officially reconvene at 1:00 p.m. Committee members, please do not discuss the meeting topic during the break amongst yourselves or with any members of the virtual audience. Again, the meeting will resume to the general public at exactly 1:00 p.m., but we ask that you join at 12:55.

Virtual Breakout participants, please be aware that it will take the entire 15 minutes to get everyone situated in their rooms. Also, when you join the Zoom platform, you may be placed in a waiting room until you are placed into the Zoom

platform. AV staff, please proceed with closing the webcast. Thank you everybody. See you soon.

Virtual Breakout Summations

Dr. Roy: It is now 1 p.m., and the Committee has returned, and I'd like to resume this Committee meeting.

We will now begin our Virtual Breakout Summations. The summations will reflect the major themes that were discussed in the Breakout Rooms in response to the scenario questions. The summations will not be transcripts of the discussion, but instead highlights from the discussion. FDA moderators, please state your name before speaking. Also, once the final moderator reports out, if there are additional points that were not covered, please feel free to use the Zoom hand— The hand raise function and I will call on you to add additional input.

So, at this point, I'd like to ask the moderator from Breakout Room 1 to summarize your room's discussion.

Dr. Bajaj: Hi, my name is Anita Bajaj. I was the moderator for Breakout Room 1. My question was, “Who do you think should be the main point of contact to educate you on the informed consent of a clinical study?” The comments included that there should be a contact information provided within the document, so that people would know who to go to with questions. Also, a suggestion of a help line was suggested, because a person's personal physician might not have the information that was needed. It was also commented that if another language was spoken, an interpreter could be needed. There was a comment that the clinic should follow up with each person, and that the document should state to the potential subject to bring their questions to the next appointment. And then one person commented that they wanted— They would

have liked their own personal physician, like the cardiologist in this case, to be the contact, but they realize that that might not be possible. They might not have the time, and so somebody else in the practice would be a good option. Thank you.

Dr. Burgette: Hello, my name is Jacqueline Burgette and I was the moderator for Room 2. I'm presenting on the question, "What information would be most important for you to see in the informed consent document?" Regarding this question, the room discussed that there are two top elements that are important to be included in the informed consent.

The first is risk benefit, and the second is obligation and rule for participation. For risk, this includes whether the study device is as safe as the existing standard of care. For benefit, this includes whether the device is less invasive than other options, and does it have a shorter recovery time. Risk benefit also included the risk of additional study procedures and additional testing that would be included by participating in the study.

The second element, obligation and rule for participation, included the length of participation; follow-up visits; if other procedures may be needed, such as the removal of the device at the end of the study; limitations to other treatment options by having this device; financial obligations; and types of support that the study will provide to study participants. This included parking, hotel, travel costs, and procedures that might be needed that are not directly related to the study.

Beyond these two elements, risk, benefit and obligations and rules for participation, our discussion also included whether the procedure for the implants had details that were important for study participants to know; rights to the data and specimens in the present and the future; who the sponsor was; who was making the device; what happens if the device is not approved by the FDA; options for continuation

of care; and who will pay for study related activities and related care after the study has ended. Thank you.

Dr. Roy: Thank you. Thank you moderators for Rooms 1 and 2. I'd like to ask the moderator from Breakout Room number 3 to summarize your room's discussion.

Dr. Gebben: Yes. Thank you. My name is David Gebben. I was the moderator for Room 3.Our specific question was, "What specific format or formats would you prefer informed consent information be provided to you for better understanding?" One of the first comments we received was that a 50-page document is a very long document. Along with that, there was an expressed concern that a preference for a video link to review the document would be helpful, as well as a simplified document, perhaps with bulleted points rather than paragraph form, would be useful to help communicate the information. It was also mentioned that sections with a FAQ section or the downsides, what information would be necessary, what personal information would be shared would also be useful to make a full decision, as also what would happen if there were parts of a device that needed to be left behind or could not be explanted if the device contained nickel, things of that concerns. And also there were concerns about having somebody directly connected to the study to answer questions along with that. And there's also questions about could there be an electronic format for providing the information. Thank you very much.

Dr. Roy: Thank you for that summary. I'd like to ask the moderator from Breakout Room 5 to summarize your room's discussion.

Ms. Gray: Are you—? You skipped four. Should I go or—?

Dr. Roy: Apologies. I'd like to ask, yes, moderator from Room 4.

Ms. Gray: Okay. No problem. So, I'm obviously the moderator for Breakout Room number 4. Our question was, "What type of information about the long-term post-study

personal responsibilities of a clinical study do you think should be included in an informed consent document to inform your decision of whether to participate in a clinical study?" So, the first concern— One of the concerns was how much will it cost me post-study in terms of the financial burden, out of pocket, and burden on my family? And how long you would be expected to have this responsibility? Is this something that insurance would cover, or would it be denied by insurance because of a participation in a clinical trial prior to FDA approval? And then, what if there's an issue with the implantable device post-study? Who should be contacted, the original study team or the current medical provider? If this is an investigational device, post-study, then what if the company goes under? You know, who would I contact once again? And what if the company is no longer there? Who would be responsible for explanting an implanted device if there are issues for severe side effects post-study? And then if I move, who do I contact regarding the device post-study? Again, you know, this is related to post-study. And what are my legal rights post-study? Do they change versus those stated in the informed consent? If the consent is continuously collecting my data after the clinical trial, what happens to this data and how does it impact me? For example, where's my data kept? Is it protected, and will it be shared publicly? And can it affect my health insurance?

Dr. Roy: Thank you for that summary from Room 4. I'd like to invite the moderator from Room 5 to provide a summary.

Dr. Grossman: Thank you. I'm Cyndi Grossman, and I was the moderator for Room 5. Room five's question was, "What concerns do you have about the personal responsibilities you will incur following the completion of this study? And do these concerns influence your decision on whether to participate in a clinical study? Please explain." The themes that came out and were noted are the longer-term implications

should be laid out in the consent form. For example, with implantable devices, about battery maintenance and possible surgeries, was the device approved for a different indication, or is it an entirely new device? As this may matter for insurance coverage after the study ends. To make anticipated adverse events clear and have a plan to help cover costs if long-term adverse events occur. Also, acknowledge when there's uncertainty about whether or not adverse events will occur long term. This is to avoid surprise costs to patients. Will I be able to afford this down the road, or will somebody be able to help? Clearly laying out all the obligations once the trial ends in terms of the support and ability to reach out to the study teams. If the study investigators find out more about the device after the study ends, will the participant also find out about that? Will they be informed about any data breaches or data integrity issues? Will the usage of data from the device continue to be followed after the trial or not? And also, finally, is there going to be interoperability between devices? Is that a possibility or not? And would the device need to be replaced if interoperability, or the ability to connect multiple devices within the same participant, becomes a possibility? Thank you.

Dr. Roy: Thank you for that summary. I'd like to ask the moderator from Breakout Room 6 to summarize your discussion.

Dr. Moazzam: Good afternoon. Caroline Moazzam, moderator for Room 6. Our group, in addition to the comments that were brought up in Dr. Bajaj's room, had additional concerns about the statement that the informed consent would be sent to the patient, and the patient would be asked to sign the form and bring it with them to the first meeting. Our group felt very strongly that there should be either an in-person or an official way to contact a representative of the study, who was informed and knowledgeable about the study and its procedures, as well as someone who has been trained on discussing medical issues at a level of eighth grade or below with patients in

so-called plain language. Our group additionally repeated many of the things that Dr. Bajaj's group were concerned about as well in regards to 50 pages being inappropriate and not accessible for enrolling subjects. Thank you.

Dr. Roy: Thank you for that summary. I did have a little technical difficulty hearing that, but I think we captured everything. I will—

Dr. Joniak-Grant: I'm sorry. Could you possibly summarize it? Because I only caught about a sentence of it.

Mr. Veizis: You know what we could do, maybe? Caroline, could you stop your video, not your microphone. Unmute your mic and try restating that. That might help open up the bandwidth a little bit.

Dr. Moazzam: Hi there. Thanks so much and sorry for that technical issue previously. Hopefully you can hear me better now. This is Caroline Moazzam. I'm the moderator for Room 6. Our question was, “Who do you think should be the main point of contact to educate you on the informed consent of a clinical study?” Our group emphasized several of the points brought up by the moderator of Group 1, Dr. Bajaj, but additionally, our group also had concerns with the recommendation that this document be signed and brought to the first visit of the study. Our group felt very strongly that there should be a designee, if not the principal investigator, then an accountable designee that was accessible to any subject that wished to enroll to answer questions, to invite and answer any questions that a potential subject may have. They felt strongly that this person should be well versed in both the procedures of the actual study, but also have specific training on how to speak in so-called plain language and discuss in an eighth grade or below level of communication. I believe that summarizes our room.

Dr. Roy: Okay. Thank you for that. Thank you for repeating that for us as well. So, now we will move to— I'd like to ask the moderator from Breakout Room 7 to provide the summary.

Dr. McKinney: Hello there. My name is Zach McKinney and I was the moderator for Room 7. We also had a discussion on Question number 2, which was "What information would be most important for you to see in the informed consent document?" And we experienced some overlap with the points highlighted by Jackie in her summary of Room 2 regarding the the importance of the risks and also the potential benefits of participation. And we also heard that, from patient's perspective, there is an interest in knowing the purpose of the study and the costs associated with participation, and whether there will be compensation to participants as well as details about the length of study participation and what's expected of participants in terms of that participation, and whether there is a placebo or control group in the study. And we also heard the call for clarity in disclosing to potential participants if there are any travel requirements associated with the study and if so, will that travel be reimbursed and if there are any limitations regarding distance for which they're eligible. And we also— Finally we got a comment, a response to the scenario itself about how travel itself can be a barrier to participation. And of course, the length of the informed consent document as a barrier. And that's all on Question 2.

Dr. Roy: Thank you for that summary. I'd like to ask the moderator from Breakout Room 8 to summarize your room discussion.

Ms. Meeker-O'Connell: Good afternoon. I'm Ann Meeker-O'Connell and I was the moderator for Breakout Room 8. We also addressed the question of "What specific formats would you prefer informed consent information be provided for better understanding?" And I would say our discussion fell into four themes. The first was key

information or some other way to break out the critical information that was most important to informing participants. The second is really the visual display of information. So, some format other than just a long paper document. These range from illustrations, to animations, to hyperlinks, to PowerPoints, and it was deemed to be particularly important when considering individuals who may have visual or other impairments. The third area was dialog. That in a modern day, we have an ability to convey information, for example, through a Zoom platform, and that people felt that that engagement could help provide a deeper context on what was in the document itself. And the last area we touched on was really a reminder to consider language in terms of format, thinking of potential participants for whom English may be a second language, as one area to to think about, and also just the complexity of the language. I think it was noted that there are some areas where the format becomes highly technical, where there are, for example, disclosures appended. So that summarizes our discussion. Thank you.

Dr. Roy: Thank you for that summary. I'd like to ask the moderator from Breakout Room 9 to summarize your room discussion.

Ms. Perreras: Hi, everyone. My name is Lexie Perreras, and I was the moderator for Room number 9. In that room, we discussed Question number 4, which asked “What information about the long-term personal responsibilities of a clinical study should be included in an informed consent document?” There are five major comments that came up within our discussion. So, the first one was that follow-up information should be included in the informed consent document. This follow-up information could include what long term follow-up is, why it's important, and what is expected of the participants or their caregivers. It could also include how long the follow-up may be for, and any protocols for staying in touch if, for example, they happen to move. Second, there

should be information that clarifies what the cost or burden is upfront, for example, at the top of the document. This information should not be buried in the document. Next, there is discussion that there should be information about what the risks may be of not maintaining the device. For example, if they stop using the device, will it cause worse consequences for the individual? Additionally, is there an option if they can't maintain it? For example, could the device be removed? We also heard that there should be information about long term effects and adverse events. For example, if there are adverse events, what is the individual's responsibility and what would be covered as part of the study? Participants shouldn't be left hanging on this. And then lastly, the informed consent document should include information regarding other products that are similar, and potentially what were their minor or major complications. This could be included as a link in the document, for example, if there's not enough space. And that was— And that concludes the comments from this group.

Dr. Roy: Thank you for that summary. I'd like to ask the moderator from Breakout Room 10 to summarize your room discussion.

Dr. Zhang: Thank you. This is Caiyan Zhang from Room 10. I'm the moderator for that room. Our room was assigned Question 5, which is “What concerns do you have about the personal responsibilities you will incur following the completion of this study? Do these concerns influence your decision on whether to participate in a clinical study? And please explain.” So, based on the group discussion, our group, I think, largely echoed the comments summarized by Dr. Cyndi Grossman from Room 5. Particularly, there might be some considerations about the uncertainty around the benefit risks, including the effectiveness of the treatment that would go beyond the specific clinical study, and also the financial obligations for long term that the patients might need to pay out-of-pocket for their health care. Additionally, I will want to add

that some participants from our room mentioned that one of the factors that they will need to consider whether they want to be a part of the clinical study in the informed consent, is that they would want to know whether there will be follow-up cares after the trial. Thank you.

Dr. Roy: Thank you for that summary. I'd like to thank everybody who participated in today's Virtual Breakout Sessions, and I'd like to thank all the moderators for your summations. At this point, I'd like to ask moderators to raise their hand if they have additional comments that they'd like to provide that haven't already been covered, and I will call on you as I see your hands raised. Okay, seeing there are no additional comments to add there, let's—

Ms. Williams: Hi, Dr. Roy, this is Letise Williams, DFO. There are a couple of hands that are raised. I believe Cyndi raised her hand first.

Dr. Roy: Oh, there you are, Cyndi. I apologize for that. Thank you so much. Thank you, Letise. Cyndi, please.

Dr. Grossman: Thank you, Dr. Roy. So, there were just two additional comments. The first was from Question 1, "Who do you think should be the main point of contact to educate you on the informed consent of a clinical study?" And our Breakout included a comment on the information from a peer with the same experience, as in a peer navigator. The second additional comment is what specific formats is— To Question 3, "What specific formats would you prefer informed consent information be provided to you for better understanding?" And our Breakout had a suggestion for standardized format, so that everybody can have the same format and it levels the playing field. That's it. Thank you.

Dr. Roy: Thank you for that. Next, I see Tracy Gray.

Ms. Gray: Hello. I'm a moderator for Breakout Room number 4, but we had some additional comments on Question number 1, “Who do you think should be the main point of contact to educate you on the informed consent of the clinical study?” The response was the research coordinator as opposed to the principal investigator, because they speak in a language— In lay language, and they're more concerned about meeting the needs and concerns of patients such as visit structures, and they're less worried about liability on the patient. Principal investigators are more invested into the scientific details regarding things such as biology and mechanism of action, and how the device will work for a given condition. While the coordinator should be the main point of contact, the investigator should be available for more detailed scientific conversations.

We also had additional comments for Question number 3. “What specific format would you prefer informed consent to be provided to you for better understanding? Comment about how people learn in different ways and communicate differently.” And so, the informed consent should occur in different formats so that they're beneficial using things such as text videos and graphics.

And going to Question number 5, the last additional comment we have on Question 5 about “What concerns do you have about the personal responsibilities you will incur following the completion of this study? Do these concerns influence your decision on whether to participate in a clinical study? Please explain.” There were comments about whether long term data is available to help inform the participant of the safety. Is it effective for one year versus five years? What is the shelf life of the device? Knowing that information would be important and would influence the decision of whether to participate. There are fears about participating without having guidance on a consent form about the study information.

However, there is a willingness to participate that's dependent on interactions with the study team, taking into consideration what was discussed, about financial and non-financial costs and burden and data collection. They also said understanding the security and privacy of the data, of the participants data, post-study and whether or not it's protected at that time, and what the implications would be that would impact their decision to participate as well, and also whether or not the device is collecting real time data during the clinical trial. And that concludes my remarks. Thank you.

Dr. Roy: Thank you. I see a hand raised from Zach McKinney.

Dr. McKinney: Yes. Thank you. In Room 7, we had a couple of other points that I wanted to add in response to the long-term implications and considerations, one of which is costs, which were mentioned previously. We had a particular recommendation that there be some sort of pre-certification process regarding insurance coverage. We also heard about the scenario of medical complications and the potential need for removal of the device. It should be very specific as to who is responsible, both in terms of the medical care but also, of course, the costs. And then in regard to the long-term risks and benefits of participation, we heard of mental health highlighted as an additional aspect, apart from whatever the direct physical clinical benefits may be, and considering the experience of participation and how that might affect one's mental health, considering the time and emotional investment in participation in the trials.

Dr. Roy: Thank you. I see a hand raised from Jacqueline Burgette.

Dr. Burgette: Thank you. So, my name is Jacqueline Burgette, and I'm the session moderator for Room 2. Regarding Question 3 about the informed consent format, my room discussed including discussion prompts. These are questions that potential participants can ask the study points of contact to facilitate dialogue. These prompts can be presented to potential study participants in different formats, such as at the end of an

informed consent video and at the end of a short summary of the study in a written consent. Thank you.

Dr. Roy: Thank you for that. Next is Ann Meeker-O'Connell.

Ms. Meeker-O'Connell: Yes, thank you. Ann Meeker-O'Connell, I was the moderator for Room 8. We also touched a little bit on Question 1 about the main point of contact. One of the comments that came up was that, often, informed consent encourages people to reach out to friends or family, but for a particularly technical study, they may not be able to be the best resource. So, there was a suggestion that another trusted, objective source could be a patient advocacy group, who can play a role in really helping to connect with others involved in the study who may be able to help explain for that particular patient. So, I just wanted to add that. Thank you.

Dr. Roy: Thank you for that comment. Next hand raised is Caiyan Zhang.

Dr. Zhang: Thank you. This is Caiyan Zhang, I'm the moderator for Room 10. Our room would like to add to Questions 1, 2, and 3. For Question 1, asking about the main point of contact for educating the participant on IC of the clinical study, some participants from our room expressed that they would like the physician who is responsible for the primary care to take on that role, because they know the best of the patient's medical history and they have the best trust from the patients. Additionally, someone also mentioned that they would like to have someone very versed in the actual care of the patient, anyone besides the principal investigator or research coordinator, but really it can be anyone on the care team where the care will be provided and then who would also need to be flexible, available, and able to answer questions for the patients. For Question 2, regarding the most important information that needs to be in the informed consent, some participants in our room expressed that they think it's really

important to walk through the informed consent with the patients. The literal words they used were "no blind spot."

So, everything in the IC is important to them. Additionally, someone also mentioned that they would prefer the risks and benefit information to be laid out right next to each other, so that would be very helpful for them to make the decision. Regarding Question 3, which is the informed consent format for better understanding, some participants in my room said that they would prefer to not have multiple formats about the informed consent on the same content. So, the informed consent itself should be really self-contained, so they don't need to watch a video and then go back to sign another paper, which would increase the patient's burden. Additionally, someone expressed that they would prefer less paper-based informed consent to help minimize clutter. Thank you.

Dr. Roy: Thank you for providing that. And I have another hand raised from Lexie Perreras.

Ms. Perreras: Hi, this is Lexie Perreras, and I was the moderator for Room number 9. We want to add to Question number 1, which was about the main point of contact and— Or who should be the main point of contact to educate you on the informed consent of a study. And in our group, the additional comment was that the person consenting should not be financially incentivized to sign up participants. And that's all.

Dr. Roy: Thank you. I don't see any other hands raised. Are there any other hands? Am I missing anybody?

Ms. Williams: It looks like— Hi, this is Letise Williams. It looks like Zach has his hand raised, from moderator seven. Moderator of Room 7?

Dr. McKinney: Yes. Thank you, Letise. And one more point that we highlighted in our Room 7 that I'm not sure was clear in my prior comment was the need for information about a variety of different possible scenarios, medical scenarios that could occur in the long term, which included the need for device maintenance and also procedures for the long-term monitoring for any potential adverse outcomes beyond the completion of the actual study. So, thank you and apologies for any overlap.

Dr. Roy: Thank you for that. And again, Letise you may be seeing things that I'm not seeing on non-video participants. Other hand raises that I'm not seeing.

Ms. Williams: Hi, Dr. Roy. Letise Williams. No, I do not see any more hand raises from the moderators, so I think we can proceed. Thank you.

Open Committee Discussion

Dr. Roy: All right. That's great. So, the summations have ended a little early. So, we will have an Open Committee Discussion and clarifying questions from the Committee now. As a reminder, although this portion is open to public observers, public attendees may not participate except at the specific request of the Committee Chair. Additionally, we request that all persons who are asked to speak, please remember to identify yourselves each time. Again, this helps with the transcription. So, let us begin and I will ask if anyone on the Committee has clarifying questions for the moderators. And please, raise your hand. And Letise I'm going to ask for your help in identifying hands raised that I'm not able to see.

Ms. Williams: Yes.

Dr. Roy: Any questions from the Committee?

Ms. Williams: All right, Dr. Roy, it looks like there are no questions to the moderators. This is Letise Williams again.

Dr. Roy: Thank you.

Ms. Williams: Oh, wait a minute. I spoke too soon. Dr. Jijo James has a question. Thank you.

Dr. Roy: Thank you. Jijo.

Dr. James: Thank you so much, Dr. Roy. We may not have details on this, but a common theme that I picked through all the discussions were around insurance. Were any of the moderators able to double click on that and get additional details, be it around experiences or concerns?

Dr. McKinney: I'm not sure I can comment— So, this is Zach McKinney from Room 7. I'm not sure we got into specific concerns, but I do remember a comment in our room that there may well be different aspects of participation or care that might be differentially covered by insurance. And so, that it would be important to understand not just "Is there insurance coverage? Yes or no," but rather what are the particular expenses and the elements of the study that will be covered or not covered, or partially covered, by insurance.

Dr. Roy: Thank you. I believe there's another response to this point. Cyndi?

Dr. Grossman: Yeah, I think— Cyndi Grossman from Room 5, moderator for Room 5. I think the comment was made that in the cases of a device that has been prior approved, even if in a different indication, that that would potentially— I think there was an assumption made maybe that that would be more likely to be covered under continued use by insurance, as opposed to a device that had not been approved, that was a new, completely new device, and under investigation. But we didn't double click beyond that comment.

Dr. Roy: Thank you. So, next question from Committee member is Meg Doerr.

Ms. Doerr: Hi. Thank you. This is Meg Doerr. I have a question for the moderators. It seemed from your remarks that there was a fairly wide spectrum of opinions that were expressed within your discussion rooms. I just wanted to check that perception with you. Did you find any elements on which there was immediate and complete consensus, or was there really a broad diversity of opinions expressed in each of your Breakout Rooms?

Dr. Roy: So, I will invite moderators to, maybe raise your hand so that I can see you, and call on you just so we don't all speak at once. So, whoever would like to answer that question. And if you're not on video, I can't see you raising your hand. Jacqueline?

Dr. Burgette: This is Jacqueline Burgette, and I was the moderator for Room 2. There was one area that we had a difference in opinion, and that was who the point of contact is for the study to do the informed consent. There were some benefits to having it be the principal investigator, being someone who has a fuller scope of what is involved for— Who has the expertise on all elements of the study. Yet, on the other hand, there are benefits to having the person of contact be the study coordinator, so then we can avoid a conflict of interest with the person doing the procedure or having a vested interest in study participation, and can maybe answer a broader range of questions versus just the technical questions related to the surgery or the procedures. So, there was a difference in opinion on who the point of the contact was for the informed consent.

Dr. Roy: Thank you. David Gebben?

Dr. Gebben: David Gebben, moderator for Room 3. And about our question regarding the specific format, there was very quick agreement and consensus that 50 pages was a very long, perhaps too long document. Thank you.

Dr. Roy: Thank you. And Tracy Gray?

Ms. Gray: Hi. I'm speaking— I was moderating Breakout Room number 4. While we had consensus on most things, there were— It wasn't like people were at odds. It was pretty much just sharing broad, different perspectives. And there was no one that really disagreed with what someone else said, but would add on to that perspective. So, does that answer the question?

Ms. Doerr: This is Meg Doerr speaking. This is really helpful to me. The reason I asked this question was to understand from the public discussion the range of opinions and the diversity of perspectives that were captured in those conversations. And it sounds like there was a diverse set of opinions that were expressed with some elements of consensus that arose. So, thank you all for that clarification.

Dr. Roy: Thank you, Meg. Next Committee question I saw was David White.

Mr. White: Thank you, Dr. Roy. This is David White, and I have a clarifying question for the moderators regarding who the point of contact would be if prospective participants had any questions. And I'm sorry if I missed this in the summations, but I was wondering if the concept of anonymity of the people asking the questions was discussed in any of the Breakouts.

Dr. Roy: So, I'll call on moderators if you'd like to raise your hand to answer David White's question. Moderators on anonymity question? Zach?

Dr. McKinney: Thank you, David. We did not discuss anonymity, but we did also hear in our room that there was a desire to ask questions of the patient's cardiologist who had referred them to the study, but who was not part of the team. And we did not get into the particular limitations on whether that is part of standard and appropriate practice. But I think the point, though, is that there is a definite interest in being able to consult with one's physician as part of the informed consent process.

Dr. Roy: Thank you, Zach. Another response from Cyndi Grossman.

Dr. Grossman: Cyndi Grossman, moderator for Room 5. Our discussion did not include anonymity per se, but it did highlight a concern about a power dynamic and wanted a point of contact, suggested a point of contact that was either a peer navigator or the study coordinator, but someone who was not necessarily an expert or maybe the lead of the study in order to have somebody more sort of peer to peer or at a level in which the participant felt more comfortable.

Dr. Roy: Thank you, Cyndi. Next response from Tracy Gray.

Ms. Gray: Tracy Gray, moderator for Room number 4. So, we did have— The research coordinator was identified as the person that would be preferred by one of the participants because of their ability to speak in lay language and really consider the burden on the patient's experience. But then another participant also felt that it was still important to have the principal investigator to provide the scientific and more detailed scientific conversation to have that with them and have that expertise available.

Dr. Roy: Thank you. Next response from moderator Ann Meeker-O'Connell.

Ms. Meeker-O'Connell: Thank you. Ann Meeker O'Connell, moderator for Room 8. We also did not talk specifically about anonymity. A little bit of a different framing in that what we heard was that while the informed consent may have a contact for questions to somebody who's a potential participant considering a particular study, that may be a stranger they've never met, and so they may be reticent to leverage that contact information. And instead, again, this is where we got into the discussion of who might be that trusted, objective source of information. I hope that was helpful. Thank you.

Dr. Roy: Thank you. And next response to that question from Caiyan Zhang.

Dr. Zhang: Thank you. This is Caiyan Zhang, the moderator for Room 10. We did not specifically discuss about the anonymity as well, but one thing that came up was one participant mentioned that they prefer their physician for the primary care would be

the point of contact to educate them about the IC for the clinical study, while it was being mentioned by some other participants that the IC might not be accessible to their primary physician for their care, but maybe the information that's only accessible by the study team. That's why the participant also mentioned the reason why they want their physician to be the point of contact for the IC is largely because of their knowledge about the medical history, and that they trust their physician.

Dr. Roy: Thank you. Thank you. I don't see additional responses to that question. And so we will move on to the next Committee member with a question, and that will be Mr. Ian Burkhart.

Mr. Burkhart: Hello. This is Ian Burkhart. I have a question just briefly, and I apologize that I forget who and which Breakout group it was that mentioned this, but talking about the main point of contact and the person that was presenting the informed consent not being someone who has financial benefit with enrollment. Was there any discussion on what defines financial benefit?

Dr. Roy: And a moderator would like to answer that question?

Ms. Williams: Hi, Dr. Roy. Letise Williams. It looks like Lexie has her hand raised.

Dr. Roy: Yeah, I do not see you, Lexie. Okay. Thank you. Lexie?

Ms. Perreras: Hi, this is Lexie Perreras, and I was the moderator for Room number 9, where we discussed this topic. I don't think we have details on specifically what we meant by financial incentive. The discussion surrounded around how some sites are contracted as clinical trial sites, and they're getting compensated for a set number of participants. And if those individuals aren't consented properly, they may be more likely to drop out. And so, the discussion really centered around that and not necessarily around specifically what an amount or format or anything like that.

Dr. Roy: Thank you, Lexie. Jacqueline?

Dr. Burgette: Thank you. This is Jacqueline Burgette, and I am the session moderator for Room 2. My room did not specifically discuss financial interest, but we did discuss perceived conflict of interest. So, the discussion revolved around the principal investigator may have a perceived conflict of interest and may not be the preferable point of contact for informed consent, yet a study coordinator may be seen as someone who does not have that same perceived conflict of interest, so they may be preferable, and also may have more time available to answer those questions compared to the principal investigator who may have less time. Yet, on the flip side, the principal investigator may have more of an overwhelming responsibility for the study and then be more forthcoming, or may have a better technical base or understanding of the study to answer the questions of the participant.

Dr. Roy: Thank you, Jacqueline. Any other responses from moderators for that question? Okay, I'm going to move to Committee questions. I do see three Committee members with their hands raised. Adam, Elizabeth and Necie. And we will go in that order. Adam, your question please.

Dr. Berger: So, I think Elizabeth was up before me, but—

Dr. Roy: Oh, apologies. Let's move to Elizabeth, then. Thank you.

Dr. Joniak-Grant: Thank you. It's okay, but thank you. Elizabeth Joniak-Grant. I actually have two questions. The first one is there's been a lot of discussion of sort of the what and how of consent. I was wondering from the moderators if there were any discussions regarding the when and where. So, sort of issues of timing, you know, in pre-op, maybe not the best place, different things like that. And then also the "wheres" of consenting, whether private offices in your doctor's office and those types of topics, if any of that came up.

Dr. Roy: So, looking for moderators with responses there.

Ms. Williams: Hi, Dr. Roy. It looks like Zack has his hand raised as well as Anita.

Dr. Roy: I see that now. Thank you for putting your cameras on. I can't see virtual hand raises without the video on. So, apologies for that. Thank you. We'll go with you, Zach.

Dr. McKinney: Thanks. This is Zach McKinney, Room 7. And thank you, Elizabeth, for jogging my memory. We did have a comment in our room that in view of the length of the informed consent document and also the potential that participants might be located at some distance from the research site, that it would actually be advantageous to have the option to do the initial question and clarification regarding the informed consent, virtually.

Dr. Roy: Thank you. Zach. Anita?

Dr. Bajaj: Hi. Anita Bajaj, I was the moderator of Room 1. I don't have an answer for the where part, but for the when it did come up that in the course of an acute illness or when somebody is not able to give their best attention, it would not be the ideal time for obtaining informed consent.

Dr. Roy: Thank you. Anita. Any other moderators with a response to this question? Okay. Seeing none, I'll move to our next Committee members question and sending that over to you—

Dr. Joniak-Grant: I'm sorry to interrupt. I'm seeing moderator for Room number 6 has her hand up.

Dr. Roy: Okay.

Dr. Joniak-Grant: And I did have one follow up question. Thanks.

Dr. Roy: Okay. Thank you. Thank you for that clarification. So, we will go to moderator 6. Caroline?

Ms. Moazzam: Hi, Caroline, I'm a moderator for Room 6. Please let me know if you cannot hear me. We did not address the when. We did have a conversation about the importance of having a first contact and interaction with actual individuals from the study prior to signing the informed consent. So, the notion that the consent would be signed before first contact occurred was very much decided upon in our room as a bad idea.

Dr. Joniak-Grant: Thank you so much. Elizabeth Joniak-Grant. And then just my second question, which is very brief. There's been a lot of talk about the main points of contact. In the moderator's view, what about an idea of someone who would serve almost as a patient liaison? Their job is to do informed consent and to be aware of the details and also have the specific training that some people mentioned. Do you think that that is something that people—That would work well based on what people were saying? Not so much? Just general comments.

Dr. Roy: Cyndi. Response from moderator of Room 5.

Dr. Grossman: Hi, thank you. Cyndi Grossman, a moderator for Room 5. In our group, what was really talked about as working very well was the peer navigator, and having that peer navigator be part of the study team, and thus trained or educated about the study and everything else, but also had the lived experience. And so, that was seen and commented on as a very successful, very well received model.

Dr. Roy: Thank you, Cyndi. Response from Tracy Gray.

Ms. Gray: Hi, Breakout Room number 4. And I shared this before about the research coordinator, but just in response to the question that was just posed. I just wanted to say that the reason that they suggested the research coordinator was for someone that could look at it from the patient experience standpoint and look at the burden and structure, and things that would really focus more on that. So, I guess from

the standpoint of someone that would have served in that role, but obviously not as in specifically in response to your question. So, I just wanted to provide those further insights. Thank you.

Dr. Roy: Thank you, Tracy. I don't see any other moderators. Caroline, your hand was up for a second, but I wasn't sure if that was from the previous comment.

Dr. Moazzam: I think it was addressed by the previous—Sorry. Caroline Moazzam, moderator Room 6. There was a lot of discussion about the person using plain language, but being equally versed on the actual procedures in the particular study.

Dr. Roy: Thank you. And that concludes Elizabeth's questions, so we will now move to Adam for your question.

Dr. Berger: Thanks. Adam Berger. I wanted to raise what I see as a little bit of a tension here with some of the responses that came in, noting one on the one side, 50 pages is too long for a consent, but also the other comment that was made was "leave no gaps," that all information in an informed consent is important. So, was that explored at all in any of the breakouts here? I'd love to get a better understanding from the folks that you were engaging with. How do you resolve that issue of not inflating the informed consent with too much information while also wanting to make sure that you get all the information that seems to be wanted and desired here? So, we'd love to just hear what your conversations were around that. Thank you.

Dr. Roy: Thank you, Adam. I see David Gebben.

Dr. Gebben: Thank you. David Gebben. Room 3, Breakout Room 3. We did discuss both. Yes, the length of the document, but it was also discussed that perhaps a video presentation would be a way to communicate that information, or the use of a FAQ section to more concisely convey the information. So, to your point, leave no

information behind, but perhaps think very seriously and carefully about how could that information be presented, rather than just a 50-page-paragraph, heavy document.

Dr. Roy: Thank you. David. Anita?

Dr. Bajaj: I'm Anita Bajaj, Breakout Room 1. We talked about how the most important and salient points should be kept up front and should be highlighted in some way, since it could be a very lengthy document having that in the beginning and focused on.

Dr. Roy: Thank you, Anita. Jacqueline?

Dr. Burgette: I'm Jacqueline Burgette, the session moderator for Room 2. Our group discussed a short summary and that a length of short was two pages, or maybe two to three pages for a larger informed consent that's written, and that this short summary can also include discussion points for engaging in dialog with the study coordinators at the end of this short summary. And that in addition to having this very lengthy written document, multiple forms of conveying the information as mentioned previously, such as a video graphics with maybe a Gantt chart that shows the participants flow through the study and in-depth visuals to communicate that flow of information in multiple different formats with that short summary and discussion points included in every single one of them. Thank you.

Dr. Roy: Thank you. Next would be Cyndi Grossman.

Dr. Grossman: Cyndi Grossman, Room 5. It was commented on that actually, in some cases, the key information that includes— Including the key information can actually make some of the consent forms longer. So, there was a discussion about utilizing some sort of technology or videos or other approaches. Also note that— Being able to have some sort of standardized, either platform or a set of open-source materials that then could be quickly adopted or modified based on this study might be helpful to

try to shorten some of the length. And then the final comment, that this triggers that— That I don't think I mentioned in prior comments, was the sort of regulations or rules around e-consent and use of electronic consent can sometimes be problematic or difficult for sites to implement, or difficult for teams to implement and cost funding. And so, finding, again, those open-source ways of sharing tools to be able to shorten the informed consent were suggested.

Dr. Roy: Thank you. Being mindful of time here, I had one more response to this question from Zack, and then we'll try to get to Necie's question. Ian, did you have a quick comment or was that another question? Okay. All right. Zack, proceed with your answer.

Dr. McKinney: I think the points from my room were pretty well highlighted by David and by Jackie regarding the value of different complementary supporting media, including videos and questions, pages, supporting publications as might be relevant, etc. So—

Dr. Roy: Thank you. We'll move to our final Committee member question. So, that will be Necie.

Ms. Edwards: Hi, Necie Edwards. Two questions, really brief. As a patient advocate and as someone who has participated in clinical trials, I want to know briefly with all of the Breakout Rooms— If it was addressed, my apologies, I don't recall it, but any discussions whatsoever about data breaches? Because when the data is stored, in the event that there is a breach, how is that going to be reported out to protect the patient? Because I'm thinking in terms of identity theft, so much is happening when you hear about various medical institutions where there have been data breaches. And then the last question is for Breakout Room number 10. I think somebody mentioned personal responsibility, so can you clarify that a little bit more briefly? Thank you.

Dr. Roy: So, we'll start at Breakout Room 10. Why don't we start with that answer? That's a specific question to you, Caiyan Zhang. And then we'll take broader responses to your first question, Necie, is that good? Okay.

Dr. Zhang: Thank you. This is Caiyan Zhang, moderator for Room 10. I didn't catch that part, I apologize. Did you say personal responsibilities or financial responsibilities?

Ms. Edwards: My apologies. Did someone in Breakout Room 10 mention personal responsibilities or was it just financial responsibilities?

Dr. Zhang: It was financial responsibilities.

Ms. Edwards: Okay. Thank you. Disregard. Thank you.

Dr. Zhang: No problem.

Dr. Roy: Necie, would you like to just briefly restate your first question? And then we'll open that up to moderators for response.

Ms. Edwards: Yes. Necie Edwards, my first question was involving data breaches. Were there any discussions in any of the Breakout Rooms where people express concerns about that? Because whether it is electronic form or hard copy form, there have been many data breaches. So, I'm just kind of curious, has anyone expressed concern about that, or had any thoughts or consideration how that should be handled?

Dr. Roy: Thank you, Necie. Tracy Gray's response, please.

Ms. Gray: Hi, I'm Tracy Gray in Breakout Room number 4. We didn't have question— We had Question number 4 and Question number 5. We still also answered in both— In some of the responses, we touched on the data issue. So, regarding Question number 5, I will say there were— Well, they didn't mention specifically having concerns about data breaches, it was more so a comment about data in general and what's happening with the data. What will the security and privacy— What measures will be taken to ensure that the data is secure and private after the study, and

what protections there would be and the implications of those protections, and all of that could impact their decision on whether or not to participate. But regarding the— And that was similar to what they said in Question number 4, we're talking about personal responsibilities. They talked about if the device is continuously collecting data, wanting to know what happens to that data and how it would impact them, but they did not specifically talk about what if a breach occurred, but they were still more interested in knowing where the data would be kept and how it would be protected. Thank you.

Dr. Roy: Thank you, Tracy. Next response from Cyndi Grossman.

Dr. Grossman: Yes. Cyndi Grossman, group 5. We did discuss data breaches, and it was discussed that the data, that anticipation of data breach, should be included in the consent language in terms of a plan for how to contact participants around that potential— If that potentially happened.

Dr. Roy: Thank you. Next response from Jacqueline Burgette.

Dr. Burgette: This is Jacqueline Burgette, I'm the moderator from Room 2. Our group did not specifically discuss data breaches, but rights to the data and how rights to the data and biospecimens should be part of the information delivered in an informed consent, not just in the present study, but also in the future. Thank you.

Dr. Roy: Thank you. And we'll take our last response here from Room 6, Caroline Moazzam.

Dr. Moazzam: Hi, Caroline Moazzam, moderator of Room 6. Our room also discussed the importance of not just—

Dr. Roy: Caroline, if you could, please— Yeah, turn your video off. Just so we get a bit better signal that way. Thank you.

Dr. Moazzam: Caroline Moazzam, moderator of Room 6. Our group discussed not just receiving aggregate or cohort data, but also individual patient-level data and the

importance of having a clear understanding in the informed consent of when and how that data is shared with [Indiscernible 01:05:20].

Dr. Roy: I had difficulty hearing that, but could hear most of it. Did the Committee hear that response? For the most part? All right. Well, thank you. We are going to move on seeing that we are a little past time. I'm going to conclude this part of our meeting by thanking all of our FDA moderators for such wonderful work today. Thank you for your participation and all that you've done on this important topic. And we will now be moving to our Open Public Hearing. So, thank you. Thank you again, FDA moderators.

Open Public Hearing

Dr. Roy: We will now proceed with the Open Public Hearing portion of the meeting. Public attendees are given an opportunity to address the Committee and present data, information or views relevant to the meeting agenda. Ms. Williams will read the Open Public Hearing disclosure process statement.

Ms. Williams: Both the Food and Drug Administration (FDA) and the public believe in a transparent process for information gathering and decision-making. To ensure such transparency at the Open Public Hearing session of the Advisory Committee Meeting, FDA believes that it is important to understand the context of an individual's presentation. For this reason, FDA encourages you, the Open Public Hearing speaker, at the beginning of your written or oral statement, to advise the Committee of any financial relationship that you may have with any company or group that may be affected by the topic of this meeting. For example, this financial information may include a company's or group's payment of your travel, lodging, or other expenses in connection with your attendance at this meeting. Likewise, FDA encourages you at the

beginning of your statement to advise the Committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking. Thank you.

Pre-recorded Presentations

Dr. Roy: Thank you. So, the FDA has received eight formal requests to address this Committee. Speakers who submitted their request to speak by the deadline indicated in the meeting's Federal Register Notice will be given six minutes to speak.

We're going to proceed now with four pre-recorded presentations, and we will begin the Open Public Hearing with a presentation from Mary McGowan, CEO of the Foundation for Sarcoidosis. Ms. McGowan, you may begin your presentation.

Ms. McGowan: Thank you to the FDA for the opportunity to share feedback on Patient-Centered Informed Consent in Clinical Study of FDA-Regulated Medical Products.

I'm Mary McGowan, CEO for the Foundation for Sarcoidosis Research, also known as FSR. FSR is the leading international nonprofit dedicated to sarcoidosis advancing research, improving clinical trial outcomes, and providing support for those impacted by sarcoidosis.

Sarcoidosis is a rare inflammatory disease characterized by the formation of granulomas in one or more organs of the body. There are approximately 175,000 patients in the United States. 90% of those patients have lung disease, and up to 25% have cardiac sarcoidosis, which may require pacemakers or defibrillators. Sarcoidosis is a disease of disparities, and Black patients are two times more likely to have sarcoidosis, 12 times more likely to die from sarcoidosis, and are at much higher risk of dying in their late 40s or early 50s.

Sarcoidosis treatment and diagnosis relies heavily on devices. These range from X-Rays to FDG-PET, and from pulmonary function tests to pacemakers and defibrillators. The insights we are providing for your consideration come from a number of different sources.

FSR has developed extensive strategies to extract patients' concerns, needs and desires. This includes data from the FSR Patient Registry, which includes the voice of nearly 7,000 patients and caregivers from 68 countries. FSR conducts extensive surveys with our community, including a number of surveys conducted on clinical trials, a focused IRB-approved survey we provided to Black patients that resulted in a 62-page white paper and its standing-room-only congressional briefing.

Furthermore, FSR works with many other patient advocacy groups and clinician groups like our own coalition for Clinical Trial Equity that will be used to help inform the insights we share. And finally, FSR convenes numerous advisory panels that allow us to take deep dives and have focus group discussions.

I will briefly discuss four concerns and desires patients have that can be folded in the informed consent process. First of all, patients want to understand the technology being used for tests or therapies. Whenever possible, show the tools that are part of trial. Let them hold them and then ask questions. This fosters a more shared decision model of informed consent, where the patient is given information and visuals at a level where they are and in a way that is easily digestible.

Patients want to ask questions, but they need to have a better understanding of the technology at their level to do so. Early discussions matter. We have learned this, especially through our Black patients, that trust building comes from early discussions about trials long before those trials take place, and creating a space for questions to

come in over time. This is a real move away from the way consents are typically obtained.

In the same vein, a lot of our patients, again, especially in the Black community, want to involve their caregivers or their community when deciding to participate in a trial. Every informed consent document should contain an infographic breakdown that the patient can take home to allow them to discuss this with their loved ones and community.

I will close with the final request the patients have as they provided informed consent. They would like that consent to also include the option for them to get access to their data, for their own day-to-day care, and to be able and to have it available for future research.

I will close with a quote from our Black Focus Group participants, and I think it summarizes so well what patients feel about how informed consent is implemented. She said, "I think that part of trust is transparency, and doctors who are willing to tell you what they know and what they don't know, and then work with you as a member of the team. Doctors who are willing to say, let's work together. Let's find out. Let's investigate together. I think that is the most helpful."

Thank you again for this opportunity to share patient's desires for informed consent for clinical trials. I am happy to take questions or follow up with you on a separate call if you would like. Thank you again.

Mr. Kahn: Good afternoon. My name is Richie Kahn and I'm co-founder and COO of Canary Advisors. We're a patient engagement firm that works to ensure clinical trials are well aligned with what patients actually want and need. A rare disease patient and clinical trial participant myself, I thank the Committee for their interest in Patient-Centered Informed Consent.

Clinical trials, of course, are intended to be generalizable to the broader population, and informed consent is a make-or-break component of this. Informed consent is more than just a single time point prior to enrollment. It's an opportunity for potential participants and their loved ones to make educated, informed decisions about clinical trial participation and how it fits into their lives. It's also a chance for the clinical trial team to thoughtfully engage with those thinking about participating.

The informed consent process provides a chance to build relationships, establish rapport, and generate trust, though it doesn't always work as intended. Often, when patients drop out of a clinical trial, one of the areas of greatest dissatisfaction is around informed consent. Participants feel overwhelmed by the length of the documents given to them to read. They have plenty of questions and they're unsure where to go for assistance.

For those seeking to participate in research, informed consent can present a number of obstacles. Here are a few that we've encountered over the years. Typically, the informed consent document itself is lengthy, full of medical jargon, and difficult for the general public to understand. Key information is buried in the body of the document, and the information presented has not been optimized to maximize understanding. Most patients will tell you that informed consent documents can be really overwhelming. They want to know what's being asked of them, how many visits will be expected to attend, the procedures at each visit and where to go for help. But they also want to know what they can expect in return. Are they going to receive best in class medical care or study related procedures paid for this data being returned?

Accessibility is another frequent challenge in the informed consent process. Many years ago, I was talking about informed consent to a friend who has Duchenne muscular dystrophy. He frequently participates in research himself, and mentioned that

while he tends to read the entire informed consent document and understands what's being asked of him, study procedures often require a wet ink signature. He is unable to hold a pen or sign his name, or otherwise complete this critical step.

Thinking of my own experience, informed consent documents are usually not accessible for the visually impaired. An electronic document that has been optimized for a screen reader can go a long way to ensuring that participants are able to engage in any trial, whether they're unable to read a document due to vision loss, or simply prefer to take in information through audio. A screen reader optimized electronic consent is a wonderful option to offer, especially as it helps to diversify trials and make sure that they are accessible to the large proportion of the population with disabilities.

Other times, the informed consent process has not been geared towards the participants' language of choice. Recently, we had to design a solution where a caregiver consent and pediatric consent presented some interesting challenges. The caregiver spoke an uncommon dialect of a language that was rarely spoken in the clinical trial site. The patient communicated through sign language, though not a form of sign language that was spoken at the clinic. So, we worked to identify a team of virtual sign language interpreters to support a rather lengthy informed consent process. The interpreters worked with an on-site translator, and all worked to assure that the entire family's questions were answered and they were well informed. This helped to really clearly communicate to the family their needs were well understood, their preferences were respected, and they were really thought of as valued members of the clinical trial team.

Early in our scholastic careers, students begin to understand how they prefer to take in new information, so their chosen learning style may vary over time. For much of my life, I was a visual learner, but as my vision loss has progressed, my preference has

changed to learning through audio or listening. Others may prefer reading, writing, note taking, or learning by doing. Unfortunately, the informed consent is usually geared towards those who learn by reading. There isn't much room for interactivity or knowledge checks. Fortunately, a number of companies are working on electronic consent. This process provides the opportunity for customization by preferred learning style, perhaps language, interactivity and accessibility. The adoption of the technology is varied by indication and region. A thoughtfully developed plain language, electronic consent can help potential participants make better informed, educated decisions about whether clinical trial participation is right for them.

I applaud the Committee for exploring the importance of a more patient-centered informed consent process, and I look forward to seeing all the positive changes that result. Thank you.

Ms. Miller: Hi, my name is Jackie Miller. I'm a rare disease patient in Fountain Hills, Arizona. Thank you so very much for holding this Committee today, it means a lot to me. I'm 40 years old. I'm single. I'm home and walker-bound, live alone, and have no support or love in my life. Nothing can heal the challenges or losses that I've experienced in my life, but it's already in the past.

I've been a high performing executive assistant for over 20 years, capable of supporting four roles working for a health insurance company, and now can't manage or care for my own life, and went on medical leave on 6/1 and currently applying for Social Security and Medicaid, which was the safety net, and now I think it's my reality. I am not just the patient, the advocate, the caregiver, the medical management facilitator, it's just me in the waiting rooms making calls to truly know what's going on.

Who I used to be. I was full of peace, love and happiness, and light and energy and joy. I was always lifting others up, laughing. It was called "Jumping Jackie" and

"Tigger." I love to travel and the only thing I ever wanted in life was to be a mother. That was my only dream. I look at that little girl and she didn't get what she deserved—

[Extracts from videos within the recording] In the way I used to be able to move and function and think— I just came from the hospital. I had my scan, I met with my doctor and— On 7/1/2022, I was in remission and it was the day I became disabled, and then you see the progressions behind since— I just can't imagine what my life would look like if I was healthy again. I just can't wait to go walk around the block—

I had a TIA leading to an ASD closure at 32, lower back surgery at 34, meningitis twice at 35, AF and PVC ablations at 36, thyroid cancer at 36 and then my unknown rare disease followed at 38, bringing 30 pounds weight loss, hyperkalemia, hypoglycemia, IBS-D, severe tendinitis, over nerve entrapment, eczema and a long list of complex neuro— And my hyperkalemia was very serious. I was passing out, beating my head, paralyzed on the floor. Nobody could identify what was happening.

The hospital, the first ER doctor, that's where my challenges began. He told me that he deals with gunshots and bullet wounds, and that was the first time I said, "I'm not safe. I'm not okay." I couldn't walk. I was bent forward. I wasn't able to shower. I couldn't do my job. I couldn't think. I couldn't function. And I went home and I found that I had low potassium and I was discharged improperly. My second ER visit didn't get much attention and I knew I needed some potassium, FRK, and then they just let me go. My third visit, they didn't want to admit me. It was within one month— Like, I begged for admittance. I had to call my PCP— Or someone who's been by my side and ensured that my care has been cohesive.

And a lot of the challenges are that I don't get a diagnosis still. It's been off and on. It goes up and down. And then of course, getting medications approved for something that's not diagnosed is challenging. So, the FRK, that was a big one, I paid

out of pocket for a while. And then I went into just trying symptom management at seven months. And so, I couldn't function. I wasn't able to conversate. It was like as if my brain was fried, so it's like there's like electrical grids that are completely down. And so we were going to try modafinil, a narcolepsy medication. Well, it's really difficult—In network when you don't have narcolepsy, but I was falling asleep at three o'clock in the afternoon. I've never napped. Now, a year and a half, like a year later, now I do have a sleep issue that's appearing. So, I don't know, and it's really hard to track because none of my issues necessarily fit in one box. And so, that's the problem with rare diseases. Nothing looks the same. And when people see me—

But for me, I have one little bucket of energy which consists of like my physical, my mental, speech, cognition, sensory, light, sound, temperature, fine motor, focus, emotions, stress, even like holding my breath during an MRI, it all draws from the same bank. And that's why my voice is a little bit depleted, because I don't have the energy to support myself. It came to the point where I couldn't lift my body. So, even like, "What can I do?" Testosterone. Okay, that wasn't a challenging one. But with the rare diseases, we are just looking to, like, "How can I get through the day? How can I try and function?" And it was, "How can I try and keep my job?" That was my biggest thing.

That was when the medication kind of began. And that's just a little summary, like an overview. I originally took three prescriptions, four pills, and now I take three prescriptions, 21 pills regularly, 15 to 20 potassium tabs a day. And I have to track, manage, follow, and cash pay prescriptions due to denials and pre-auths. And the hardest part is not having my brain to function. And I've spent 20 to 40 hours a week before just on medication management, tracking, trying to ensure that I receive it, following, locating it.

I've been independent all of my life, I never needed support, and at nine months I couldn't do it. There's no pushing past this. This is the only time I've ever asked for help and desperately needed it. No in-person support, family or friends or anybody to kind of just like, even discuss life with and make decisions with. I'm safe, but I am at every risk for, like, increased suicide risk for being a rare disease patient, disabled, isolated and having no support. And it's so challenging.

If there was a legislative exception that could be made for rare diseases that managed care puts on medications and quantities, it would greatly improve the health of so many, remove stress, worry and anxiety, for my own safety and allow me to focus on my current and future care. Rare diseases are not standard treatments with standard doses. They often require unusual treatment strategies, and every patient's symptoms do not fit nicely in the same box. And so, it's really hard to diagnose. I've been diagnosed, undiagnosed, and then nothing doesn't matter because the treatment isn't going to get the diagnosis and change the treatment. It's mostly symptom management. I'm so grateful for your time. Thank you so much.

Dr. Collinger: Hi, my name is Jen Collinger. I'm happy to be here today to talk to you about Informed Consent for Early Feasibility Device Studies. And I'm going to share some of our experiences with running an Implanted Brain-Computer Interface Trial.

So, an Early Feasibility Study is a limited clinical investigation of a device that is early in development. Typically, it's limited to a small number of participants, and it's used to evaluate the initial clinical safety and device functionality. These studies are conducted under an investigational— FDA investigational device exemption, and these studies are often very complex and involve a large commitment on the part of the participants, as you'll hear about for our BCI study. And so, in the informed consent

process it is really important to make sure that participants have a true understanding of the study before they decide to participate.

So very briefly, the device that we're developing is a sensorimotor BCI. We use electrodes that are implanted into motor cortex to record activity from the brain. We can turn that into control signals for a device such as a robotic arm. At the same time, we can record from sensors in that robotic arm to measure forces at the fingertips, and then turn that into stimulation patterns that can be sent through electrodes that are implanted in somatosensory cortex, shown here in red, to restore the sense of touch for the participant. And this is a multi-site study that's being conducted at the University of Pittsburgh and University of Chicago, where the goal is that this is a first-in-human study to demonstrate the long-term safety and efficacy of a sensorimotor BCI. We're working with adults who have chronic upper limb impairments, who are unable to perform functional activities with their hand. And because it involves neurosurgery, this is obviously a significant risk study. At this early feasibility stage, there's no direct benefit to the participants. They are really helping to contribute to the development of devices that could benefit people with tetraplegia in the future. The study design after the device is implanted is that participants work with us about three times per week, for anywhere from 1 to 10 years after implant. So again, it's a very large time commitment for the participants.

Now I'm going to talk through some of the specific elements of our study design that we've incorporated to try to improve that information sharing and informed consent process. So, when participants contact us interested in the study, we conduct a phone screening to determine initial eligibility. And then we start to share documents like the consent form, maybe photos or videos or information on our website that's been approved by the IRB in order for them to better understand what the study involves

prior to proceeding with a consent, a formal consent. Then, we schedule some pre-consent visits where we've taken elements of the protocol, either the study procedures and key things that we want to talk about related to those, or the study risks. And they meet with two of the clinicians on our team to go through each of these in a separate visit, where we go through and answer questions about each of these, and kind of document that we've talked about some of the key procedures and risks.

We encourage participants to bring a family member or caregiver to this visit so that more than one person is hearing the information and having an opportunity to ask questions. If they are still interested in participating, we would schedule an informed consent visit, where again, we go through the typical elements of consent, discussing procedures, risk benefits, that the study is voluntary, and we obtain consent from the participant as well as from a caregiver, because there's some ongoing monitoring that will require their input. Prior to the implant itself, we actually schedule a number of visits so that participants get used to the logistics of coming into the lab, that they understand the nature of what types of tasks they'll be doing with the BCI. Some of these visits involve questionnaires, meeting with a rehab neuropsychologist to understand their expectations for the study, and make sure those align with what we're actually trying to accomplish. We do some imaging to plan where we're going to implant these electrodes. We use a non-implanted BCI, again, to expose them to the types of things that we would be doing after the device is implanted.

And then we go through a standard clinical preoperative visit to make sure that they're eligible for surgery. Our neurosurgeon will implant the device after obtaining a surgical consent, and then there's standard post-op care and training that happens after implant. The bulk of the study is really the BCI testing that can happen over, as I said, 1 to 10 years, up to five times per week. We do a monthly physical examination just to make sure that there's no changes in

function, and then they also check in quarterly with our neuropsychologist to again provide any feedback about the study, prepare them for the end of the study, and again, just make sure the expectations are aligned. And then, at the end of the study the device is explanted. We have clinical post-op care as well as follow-up visits with our neuropsychologist.

So, just to summarize some of the opportunities that complex studies might have to incorporate for improving informed consent, one is that you have the opportunity to provide information prior to the formal consent visit, so that they can start to generate questions and understand what's involved. As you probably know, informed consent documents for a study like this could be 20 to 30 pages long. And so, while it's important for them to read that thoroughly and ask any questions, something we've done is break out key points that we really want to talk through individually and have questions asked and answered about. And we do that prior to the informed consent visit, where you can include family or care partners in these discussions. We've incorporated these pre-implant study visits to help them have an understanding of what experiments in the lab or in the home would be like, and the logistics of getting to the lab. And then we've incorporated ongoing monitoring and consent, both by our study team as well as a neuropsychologist. So, thanks for the time, I appreciate it.

Open Hearing Presentations

Dr. Roy: Thank you. That concludes the record— The pre-recorded presentations. And now we will move to live Open Hearing Presentations and we will start with our first presentation and that will be from Madris Kinard.

Ms. Kinard: Hi. This is Madris Kinard. Can you hear me? Okay. I'm going to go ahead and share my screen. All right. So, my name is Madris Kinnard. I was not paid to attend today or to speak just speaking on behalf of myself and also with a little bit of

information, because at one time I worked for both Medicare and for the FDA. And I hope that this is helpful.

So, I'm focusing mostly on medical devices because most of my background is in that area. I had worked for the FDA as the UDI Program Manager. The UDI is a barcode, essentially that goes on a medical device, that can be put into the Electronic Health Record so that as you get care through your life, it's easy to know what was used for your procedure. I also worked on the Adverse Event reporting database. So when something goes wrong with— I worked on the drug database first, and then on the device one. So, when something goes wrong with a drug or device, it gets sent to this database.

So, informed consent for clinical trials is a little different than it is for devices already on the market. So, if a device is on the market, it typically would have that UDI I was talking about, which is a barcode. It can be 2D or it can be a long barcode, but it's similar, you know, if you see a recall for peanut butter, you can go look at the UPC on your peanut butter and see if it's part of a recall. But we don't really have that in place so well with the UDI. So, even though it's on the labels of the devices that are used now, maybe not for clinical trial devices, but for devices that are on the market or for devices that are used, with a surgery where you may have to have clips or staples, to hold the device in place, that is available.

And so, I think one of the things that's important is not to just talk about the device that is being implanted, but to know if there's anything else being used in the care, because things like surgical staples or clips could contain nickel. This is an opportunity for the clinical trial staff to talk to the patient, make sure that they don't

have hypersensitivities or allergies that might preclude them from being part of the study.

And one of the things I want to do is tell you, I was in a clinical trial for a drug 25 years ago, and about two months in, I actually felt it was helping me quite a bit and I got kicked out of the study and I didn't know why. This was before HIPAA was a thing, before we had rights to see our data, and I called and begged and pleaded to stay on the trial, and they said that I couldn't. And I said, "Well, what's wrong? Why can't I be included?" The only thing the person would tell me was to go see a rheumatologist. And that's how I ended up being identified as a patient with lupus. So, this was 25 years ago, and even though they probably weren't even supposed to tell me that much, they really helped more than they could know because I was able to identify the source of some of the issues that I had. So, I think one of the things to know is that it's super important that we have access to our data.

It may not be possible to have access to it through the clinical trial due to privacy or trade secret information, but at some point, you should be able to know, will I get the data that I need? Can I coordinate that data with my family doctor? Is this something that they can even know that I'm a part of? And at some point if the device moves beyond the trial, can that information go into my health record? Because trials don't last as long typically as the person is alive, one would hope. Right? So, if your trial leads to a product that goes onto the market, I would think the FDA would love to know if something happens after that trial ends. They want to know if something happened with the device or the drug and try to identify the root cause. So, one of the device registries that reports to the FDA right now, I've been looking through some of the data and I've noticed that it's for a cardiac device, but what they're pointing out is a

potential problem with an introducer. And that introducer isn't being reported on its own because it's part of this trial and it's part of a kit. But certainly, if there is a kit used and it has multiple pieces, it would be good for the patients to know what is in that. Especially, if the trial has ended and they need to continue care outside of that trial.

So, the term that I use here is going concern. And it's not one I've heard the FDA used before. It actually came from my background; I was going to be an accountant at one point. I had one year of accounting school for college and going concern is you have to assume that what you're working on is going to continue. So, assume that the product is going to make it to market and that there could be potential issues down the road and the informed consent at the beginning may not be the same as what is needed toward the end of the trial. If you know that the device now has a label and we're going to use it for this off-label use or anything to that effect that can be communicated to the patient, kind of almost like a package that you would receive at the end. This is what you need to do now because you are no longer going to be followed by this trial. Let them know what devices were used if they don't know already. And let them know if there are any risks or follow-on medical costs. Now, the medical costs would be good to know in advance, but sometimes they can't be known yet because the trial hasn't happened. And so, I think it's good to have this going concern and to realize that these are patients that you're working with and they're going to be someone else's patient when your trial ends. So, I think it's important to include in the informed consent what was used and who they should report to after the trial ends, if there is a problem. Do I report it to the FDA? Would I know how to do that? If that's expected of me. How would I know to do that?

So, a lot of trials do end before the long term for the patients because they'll last for two years or five years with the case of anaplastic large cell lymphoma for women who had breast implants, the any trials that happened ended before that was really an issue, because most times that came on around 8 to 10 years. And so those patients needed to know what was implanted in them so that they could later get help. This is just a search that I did on Adverse Events for surgical clips and staples that are used in surgeries. And so most times these aren't thought of as the primary device that's used, but they can be used with a lot of different procedures.

And so, I wanted to point out that devices that are used as part of the surgery can have issues later and so it's good to know what those potential issues could be and for the FDA to know to track them. So, at this point right now, there are about 300,000 reports and over 200 recalls for these types of devices and they actually could be leading to the failure of what was used in the trial or could lead to finding additional outcome information. And so, if the patient doesn't know or it's not in their Electronic Health Record, what was used, it can be really hard to identify that a clip or a staple could cause trouble years later.

So informed consent still applies a little bit here, because after the trial is over, what does the patient need to do. So right now the FDA has about 19 million reports of injuries, deaths and malfunctions. This goes back 25 years and the office of the Inspector General estimates that only about 14 % of adverse events even make it to the FDA. And so why would this be the case? A report of an adverse event is only going to occur when the patient or the physician or the provider knows that a device may have been used and may have contributed to something. And how will the patient know if it's

not in the EHR, if they don't remember what the device was that was used and they can't communicate that. So that was my message today.

Dr. Roy: That's wonderful. Thank you, Madris. We appreciate that. Right. Just over six minutes here.

Ms. Kinard: I'll include my slides for anybody who wants to see them then. Thank you.

Dr. Roy: Thank you very much. We'll move to our next live Open Public Hearing presentation from Ms. Laura Lytle from the National Center for Health Research. You may begin your presentation.

Ms. Lytle: Thank you. Madris, I wish I could yield some of my time to you because I'm not going to take six minutes, I don't think. Hi, my name is Laura Lytle. I'm the health policy director at the National Center for Health Research, which is a nonprofit think tank that conducts, analyzes and scrutinizes research on a range of health issues with a particular focus on prevention strategies, treatments and products that are most effective for patients and consumers. I should note that we don't accept funding from companies that are a subject of our work, so that we have no conflict of interest.

I'm grateful for the time today to share NCH's insight and to underscore the importance of strengthening patient informed consent. We applaud the FDA's effort to provide a framework to improve patient informed consent and transparency. We support the suggestions made in the FDA's draft guidance on key information and facilitating understanding and informed consent.

We wish to provide insight today on ways to codify the FDA's guidance and to provide meaningful and impactful improvements on the consent process, and to reinforce much of which has been discussed during today's session.

Number one checklist. We support the FDA's previous use of patient information checklists to ensure that informed consent for products already on the market, and urge that this model be used in clinical trials and studies to ensure that all key information is easily conveyed and understood by the patient. Short checklist consisting of a sentence or two for each key fact allows the patient to pause, digest information, and sign their initials by moving on to the next checklist item.

Process. As discussed, informed consent should be a process and not a one-time presentation of long, complicated documents filled with legal and technical terms that the patient must sign without having the time or the ability to fully understand and consent. This process should include oral, visual, and written components. Patients rarely read lengthy informed consent documents, and are more likely to ask questions during an oral discussion or video and be able to pause and consider the risks, benefits, rights and responsibilities of each clinical study.

Three key information. Key information should inform patients of details that they may or likely do not know and should be prevented— Presented, excuse me, in an order of relevance to the patient, it should inform patients of what is known and not known about potential benefits and risks in participation.

Patient privacy and access to their information is my fourth point establishing how this data is stored, who has access, and importantly, how the patient will be provided with this information during and after, as discussed at the conclusion of the

study. This is particularly important for post-market research and medical devices. I thank you all for the opportunity to speak with you today, and thank you for your efforts in providing guidance in order to improve, standardize, and inform the consent process. Thank you so much.

Dr. Roy: Thank you. We will move to our next presenter and that's Ms. Tess Robertson from the National Center for Health Research.

Ms. Robertson: Hello. My name is Tess Robertson, and I'm speaking today on behalf of the Patient Consumer and Public Health Coalition, which is an informal coalition of more than two dozen nonprofit organizations that focuses on ensuring safe, effective and affordable medical and consumer products. The coalition does not accept funding from entities with financial ties to the products that we work with and analyze. Our coalition appreciates the FDA's efforts to improve informed consent in clinical trials of medical devices, and all the suggestions made in this morning's presentations.

We support the suggestions made in the FDA draft guidance on informed consent. We also encourage the agency to make these recommendations enforceable or create incentives to maximize compliance.

My experiences in public health research and study design have highlighted the complexities of getting true informed consent from participants. True informed consent is, as many of us have discussed today, a process that should meet participants where they are, it is not just information on a piece of paper. The coalition agrees with the FDA that there is a need for improvement. We've worked with thousands of patients, and they tell us that informed consent documents are often too long, technical or confusing for them to understand.

As we all know, the longer the consent documents are, the less likely they are to be read. CDRH attempted to improve the process for devices that have been cleared or approved by using patient information checklists, which we support in the post-market environment and think would be helpful to improve informed consent during clinical trials when there are especially many unknowns about risks and benefits.

This checklist format could include numerous facts, and the patient would be able to initial each fact separately to show that they have read and understand it. The health care provider or study representative would also be able to sign the checklist to indicate that they provided the same information orally. This allows for more of a back-and-forth conversational element to the informed consent process.

However, checklists can also be long, too long and include information that may be self-evident or not obviously relevant to a patient who is trying to decide at that moment whether to sign or not. Moreover, when a sample checklist is provided by CDRH but a company is still allowed to revise it as they choose, this may not protect patients from misleading or confusing information. For that reason, a patient information checklist must include certain information in a specific format to ensure that the patient has all the key information about the trial and what is known and what is not known about the device when making their choice to consent.

Most importantly, the information that the healthcare provider provides orally to the patient should be virtually identical to the information provided, either in writing or in a consent form. Again, the average reading level in the United States is around eighth grade level, which means many Americans read below that level. The checklist, or any other information provided to ensure informed consent must therefore be simple to the point and easy to understand. Thank you for the opportunity to share our views today.

Dr. Roy: Thank you. We will now move to our final live presenter and that is Mr. David Curry, president and CEO of GE2P2 Global Foundation.

Mr. Curry: Good afternoon. I'm David Curry, president of the GE2P2 Global Foundation, a nonprofit founded in 2016 to advance scientific rigor, ethical resilience and integrity in research. Our public comment today proceeds from ongoing work in the Foundation's Center for Informed Consent Integrity. We'll focus on three areas which we believe to be extremely important, but which did not receive adequate focus in our view, in the executive summary document posted for this meeting. And we're not focused on during the excellent presentations this morning or the rich virtual session report we just heard.

These three areas highlighted on the slide are: Informed consent comprehension including measurement and mitigation, assent and secondary or future research involving stored patient data or biospecimens.

So, first comprehension. While the executive summary document uses the term comprehension some 14 times, it does not acknowledge or address some key critical weaknesses in the consent processes overall. Unfortunately, the academic literature confirms that we, the global community, do not have tested effective strategies, tools, or techniques to meaningfully or consistently measure comprehension of informed consent information. Rather, we have a number of measurement models that are in various stages of evolution, such as the teach back approach referenced by Doctor Morales this morning, for example, but none, in our view, are near gold standard.

Equally, the global community has not yet articulated what thresholds Comprehension would confirm that truly informed consent has been meaningfully and effectively given, whether a consent form has been signed or not.

Finally, we do not have specific, validated strategies to mitigate deficits which might occur in informed consent comprehension. Such strategies would ideally enable a potential patient or trial participant to improve their comprehension to levels which would allow their responsible enrollment in a clinical trial. The Advisory Committee might consider recommending that FDA focus appropriate resources to study consent comprehension, its measurement and mitigation strategies, all to advance patient centered consent overall.

Second area: assent. We believe that consideration of patient centered consent must also address asset empowering younger persons who do not have legal standing to fully consent, as well as persons who may have transitory challenges in cognitive functions, such as from an injury, or who may experience other cognitive challenges across the life course. Meaningful assent involves all the issues around comprehension we noted a few moments ago, but also involves complexities around parental, guardian and caregiver roles and, for example, the right to refuse participation, even if participation is consented to by others, is often overlooked or given inadequate focus in discussions around consent role. Indeed, we note that this meeting's executive summary document does not use the term assent even once. We also note that across the six excellent presentations made this morning, assent was not mentioned. The Advisory Committee might consider recommending that FDA focus appropriate resources to more fully articulate how assent can play its full role as a dimension of patient centered consent.

Finally, third secondary or future research. There is a rapidly growing body of clinical research which utilizes patient data and or biospecimens originally captured during an earlier clinical trial. Such research can occur well after the original trial and focus on questions which may or may not be directly related to the questions in that original trial. Also, such research is able to consider new kinds of scientific questions enabled by growing biobanks and data repositories of patient information and driven by new tools such as generative AI. The consent and assent issues here involve ensuring that sufficiently precise information about known or potential future use of a patient's data, or biospecimens in future research is clearly addressed in the original consent interaction, or by additional consenting at future points. Such information should well address what rights a patient can exercise, if any, to selectively modify or withdraw consent, depending on the nature of the new research focus: the research organizations involved, the sponsor or other parameters.

Finally, we note an important emerging theme in global clinical research ethics guidance involves non-clinical forms of benefit that is just not risk and benefit for the patient in the original trial. These might include benefits such as intellectual property or non-trial related compensation, which might depend on outcomes that proceed from this future, or secondary research which utilizes the patient's data or biospecimen. This is a very complex issue, and it receives only a single sentence in the executive summary and was not addressed this morning.

The Advisory Committee might consider recommending that FDA focus appropriate resources to develop a robust and nuanced draft guidance or other analysis on consent and assent around data and biospecimens used in secondary or future research. These three areas comprehension, assent and consent for using data or

biospecimens in future research deserve much additional coverage. I appreciate your attention and happy to take questions in the next part of the meeting. Thank you.

Open Committee Discussion

Dr. Roy: Thank you for that, Mr. Currie. So, at this time, I would like to thank all of today's Open Public Hearing speakers. We truly appreciate your willingness to share your perspectives with us today and so I will now pronounce the Open Public Hearing to be officially closed. We will now proceed with today's agenda. And so, with that said, we're just we're right on time and we are going to move to the Open Committee Discussion, clarifying questions from the Committee.

So now we will have these Open Committee Discussion and clarifying questions sessions. As a reminder, although this portion is open to public observers, public attendees may not participate except at the specific request of the Committee Chair. Additionally, we request that all persons who are asked to speak identify themselves each time. This helps with the transcriptionist. And as a reminder from me, I cannot see your electronic hand raised if your video is not turned on. So, with that said, let us begin.

And does anyone on the Committee have any clarifying questions for the Open Public Hearing speakers? Again, please turn on your video monitors, unmute your phone, state your name when you're speaking, and use the Zoom hand raise function and I will call upon you. Thank you. So, Committee member questions. Terry Diaz.

Ms. Diaz: Hi. Terry Diaz. So, I have a couple of questions. My first one, I will say is for Jennifer only because you were talking about the long-term study that you are

doing and I wanted to know, how do you make sure that your participants fully understand the benefits and the procedures that you're doing for that long term?

Dr. Collinger: Sure. This is Jen Collinger. Thank you for the question. You know, I think we try to do that just through repeated discussions with multiple members of the team. And so it offers a chance for them to hear it explained by multiple different people to ask questions. We invite them to include a family member or care partner in those discussions. And then once they are enrolled in the study, they also meet with study personnel, clinicians once a month to discuss ongoing expectations and changes and they meet with the study psychologist every three months, who's a little bit removed from the team to address any questions.

Ms. Diaz: Thank you. That answers my question. And then the second question I have is, for any of the presenters, what do you find to be the most challenging aspect of implementing informed consent with patients?

Dr. Roy: And anyone who'd like to respond to that, please raise your hand.

Dr. Roy: Yes. Richie Kahn.

Mr. Kahn: Sure. So, I think one of the most challenging aspects around informed consent generally, I think, is changing how it's thought of in general. Right? So too often informed consent is really thought of as a tick box instead of an ongoing opportunity, a process that's really all about building relationships and rapport with patients. So that, for my money, is the greatest challenge. Making sure that the time spent between coordinator and potential participant is really meaningful and used to build relationships.

Dr. Roy: Thank you, Richie. Would anybody else like to comment on that topic?

Dr. Roy: Yes, Mary.

Ms. McGowan: I would just agree with that. And to add to that, I think it's just the complexity of it all because it is, you know, somewhat scary process for patients, for many of them, a new process. I think they're looking for some support in this area and not quite sure where to turn to.

And so I think anything that we can do to help clarify that for them and support them in those efforts, I think is really a great opportunity. And I would agree with what Richie said. You know, it's a conversation, it's a building it into the process early on. That really builds trust and no surprises or even potentially backing out, you know, once it's provided to them.

Dr. Roy: Thank you. Are there comments from other Committee members at this point?

Dr. Roy: Yes. Adam Berger.

Dr. Berger: I think Camille was up first. Sorry. I just don't like cutting in front of people. Apologies.

Dr. Roy: Okay. Thank you. We'll go with Camille Nebeker. Thank you.

Dr. Nebeker: Thank you. I have notes, and I didn't write names next to my notes of who said this. I'm Camille Nebeker, and I have this note that says they want to understand the technology, they want to ask questions and I'm curious about they want to hold the technologies. So, I want to know more about the technology, whether it's controlled by the research team, whether it might be a third-party technology, whether or not there's just understanding the technology, but also there's a big component to

technology that might involve data management, data collection. It could be a wrist worn sensor. So, the data that are being collected on the technology, how it's being transmitted, who will have access when it might be shared. There was a comment about a breach.

So, my question is really about data management processes and how those are explained to people in a way that's accessible. Where are the challenges in that? What are the concerns about third party involvement? To what extent is there a need to review privacy policies if there's a commercial entity involved. So that question opened up a lot of questions for me, and I'm just wanting to put that out. Thank you.

Dr. Roy: Thank you. We'll take a response from Mary McGowan.

Ms. McGowan: I'm not sure if I'm the only one who said that, but I did say that in my presentation. And the reason being, just to give a bit of quick background on this, we did an in-person training at the Cleveland Clinic and for patients. And the Cleveland Clinic was generous enough to have the patients involved in a tour of the sarcoidosis clinic there. And it was during that tour that the patients had the opportunity to hold in their hands defibrillators, wires, and medical devices that had been implanted in their bodies and many of them just broke down emotionally because nobody had ever taken the time to show them or to have them hold it, or to explain really in great detail what that medical device was that they were implanting in their bodies. And so with further discussion about that, we realized how important that is for patients, in the entire process, right? Research, situations where they have to have medical devices implanted. So anyway, I just wanted to give a little bit of background on why that was mentioned and where that came from, at least for me.

Dr. Roy: Thank you for that answer. We'll move to the next Committee member, comment or question. And that is now you, Adam.

Dr. Berger. Thanks. Adam Berger. So, I wanted to see if we might explore one topic that seems to be— Has been raised by a number of you, and this is enabling access to your data where the participants' data, you know, the common rule requires, a statement as to whether results will be returned in it. There are other requirements around this. I'd like to understand what would be the information you would need to see. And again, kind of going back to that tension between trying to make the consents not be 50 pages, how do we reduce that while still conveying the information. To all of you, what is the key information that you would want to see in a consent form related to enabling access to your data? Thanks.

Dr. Roy: Thank you, Adam. Is there a response to Adam's question from one of the presenters? On data.

Dr. Berger: So maybe I'll reframe it as a separate question. Is it simple enough to just make a statement about whether or not you will receive access to your data, or do you need more information? And I'm going to give you a little bit more context, is this information of what you know, how that information will be conveyed and what methodology, what how it will be explained to you and what potential risks that the information might actually entail. I think we heard an individual speak here that said they were able to— They were identified as someone who had lupus, right? There's all sorts of information that you can get out of this. So, I'm just wanting to know from all of you what is the minimum information you want to see around that concept of data access?

Dr. Roy: Okay. We will take that as a comment. And, Adam, we will take your questions and consider those commentary on the reaction here. Thank you for that. I see Committee member Dave White with a question.

Mr. White: Thank you, Doctor Roy. My question is for David Curry. Thank you for your presentation, highlighting things that might not have been highlighted otherwise, it is the best way of putting it and particularly my question involves the comprehension of more measurement being needed. I was wondering, which aspect of comprehension was it: the person being consented or the person doing the consenting? Both, or a combination? Or did you have other thoughts?

Mr. Curry: I've opened my mic; I assume I can be heard. Thank you for the question. I think it's fair to say that a good deal of the meeting today has been discussing all kinds of strategies, formats, media, other ways to try to support key information, how any information that needs to be conveyed in a robust, informed consent is understood. What I was trying to convey was that all of those strategies undoubtedly contribute in different ways and I was trying to recognize that, in the— If we can call it a field event, we are still a good way away from having the kinds of assessment or measurement approaches, which can tell us with some confidence which of those strategies may be helping with comprehension. Or what I was saying more directly is how we can think clearly about, you could almost call it scoring comprehension, because just to say that the informed consent was comprehended is not very precise. We don't have good mechanisms to measure it. We don't have good models or ways of thinking to suggest what an adequate comprehension score might be.

And so, I was trying to signal that we have a good deal more work to do, not just on creative ways to try to help with understanding and comprehension, but on sort of

the back side to have ways to understand whether comprehension is being successfully achieved or how we might improve it, or if there are specific deficits around a particular area risk. For example, do we have backup strategies to help a potential patient or participant improve their comprehension? Because in the end, assuming that a potential patient or participant would like to participate, we should be supportive. We just don't have the tools to tell us how well they comprehend where there may be specific deficits in their comprehension or what we can do to help them overcome deficits around particular areas, to allow them to participate in the first place. It was not intending to be about the person conducting or facilitating the consent. It is about our ability to measure and act on the measurements, person consenting or trying to consent.

Mr. White: Thank you, David. And if I didn't mention my name before, I apologize. This is David White. Thank you so much for that explanation. It sounds like we need to think more about what we're trying to measure and how, as opposed to simply brainstorming.

Mr. Curry: If you're asking me to comment that we would assess that moving more towards, I use the word precision to more precisely understand how to effectively measure comprehension. In the end, we would want and I think our federal regulations insist that persons that we enroll in clinical trials have been properly, effectively, meaningfully consented. If we don't have effective ways to measure comprehension, then we are doing that, making the best judgments we can as individuals who may be facilitating a consent transaction. We may, but we have a way to go. That was the observation. We do see in the literature. It's not as if no one's attempting to think about this, where we're able to, for example, feel confident that there are three different kinds of tools that we can use to confidently assess comprehension: making enrollment of a

given person, a responsible decision or a fully responsible decision. It's— We're on the journey. I guess it would be the most constructive way to say it. Certainly not there yet. And that's why I found today's meeting bringing the Patient Advisory Committee to the table is so important and all of the rich commentary and perspectives we've seen today are evidence of that.

Mr. White: Very well put, David. Thank you again.

Dr. Roy: Thank you, thank you. We'll move to the next Committee member comment or question. Elizabeth?

Dr. Joniak-Grant: Thank you very much. This is Elizabeth Joniak-Grant. My question is for Mr. Curry and others, of course, are welcome to comment as well. I wanted to talk a little bit more about this idea of assent versus consent. Especially, I as a patient, I've been asked to participate in clinical trials, but I did notice when my son, as a patient was asked to participate in clinical trials that asking basically was, you know, ignoring him in the room, coming straight to me and asking if I was willing for my son to participate in a clinical trial. So I am very mindful of this topic. What I was wanting to ask specifically was how, if you do— How do you see a scent being achieved sort of with children and others and how, you know, do you have ideas about what that would look like and how it would differ from consent? Practically speaking.

Dr. Roy: And, Elizabeth—

Mr. Curry: -Thank you for the question. You're asking an important question. Of course, the legal standing of younger persons to consent typically is triggered by an age, typically varying state to state, and certainly varying widely globally. And the age at which any consent can be considered also varies, and there is a fair amount of debate

and different practice about just how young a young person can be, or to measure cognitive capability for someone who might have a head injury, not necessarily present themselves as having full cognitive function, or someone who may have a life course event where cognitive capability may be in decline. All of those things may trigger the same question. I'm not sure that— I don't know what time available that he has, but certainly we are advocates for recognizing that younger persons who may not have legal standing in a given state, for example, may well demonstrate the maturity and the ability to understand information which could largely enable them to consent, even if they're not legally allowed to. And the presumption that younger persons should have no exercise of or consent, I think, is very problematic.

Some of our work over the last several years has been in the gene therapy area, for example. I know that's not device-related, although there can be areas over. And since most of that research, which can be life altering going on in young person. It is not a trivial matter to simply not give serious consideration for how assent can be and secured or given. Many of the commenters today in the presentations this morning referenced, for example, the inclusion of graphical material or video material. For all I know, musical theatrical help persons with different learning styles, different capacities, different literacy levels understand what is otherwise complex content. Those same recreative approaches to assisting adults who legally can consent but can benefit from such support, can be directly translated to younger persons who may be in a position to provide assent. I also mentioned refusal to participate, which is not assent at all, but is the exercise of an assent like— I want to be respectful of time here. I hope that's partially responsive and I depend on the meeting moderator to be.

Dr. Roy: Yes, that's that we have time for discussion here. So, thank you. Are there more questions or comments from Committee members? I'd like to pose a question and a comment to our presenter, Jennifer— Sorry. Jackie. Our patient who so eloquently and vulnerably shared her patient story with us today. And, Jackie, could you share with the Committee, maybe one or two takeaways from your experience that you would love to see, you know, incorporated into informed consent?

Ms. Miller: Everything everybody said today was so helpful to me even, like I was making notes about my devices, wondering if the nickel was in there. I really appreciate the lengthiness because as you can see, I can't manage my own care. I'm disabled and I felt so embarrassed. I just saw FDA wanted to hear, and I was like, somebody wants to listen and so what you guys are doing is beyond anything. And I work for a health insurance company, and I've had this rare disease for two and a half years, and I'm undiagnosed and I've been through ups and downs and just literally having this forum and you listening to people. And I know now to be aware of what to be engaged in, but I've fallen into these pockets because I'm so desperate. And you guys asking is everything; it really is everything. Listening, just being seen and feeling like a human being. Thank you for that. Thank you. Sorry. I don't want to go too inappropriate, but that's been the hardest part because I don't have any support. It's me and you can see my brain doesn't work and I'm all over the place just trying to find something. And being seen as a human being and an individual just means a lot. I'm so moved and proud of what you guys are doing. And just to be able to like to listen and watch. And I'm going to be watching more. I have so many new ideas and thoughts and thank you.

Dr. Roy: Thank you, Jackie. I think I'd like to just comment that all of us here around this table care deeply about patient success stories and thank you for sharing

yours with us and giving that insight and emotion and again, vulnerability that you've shared with us. I see Committee member Terry Diaz.

Ms. Diaz: I hope this is appropriate, but, just so you know, Jackie Miller, that's what I do for advocacy. So, if you want to reach out personally, you are more than welcome to.

Dr. Roy: Thank you. Terry. Any other comments? Questions from the Committee? Going once. Going twice. Alright.

If Committee members do not have any further questions or comments for presenters, I'm going to proceed here with our agenda and we're going to move on with taking our break. So, we will now take a ten-minute break. Committee members, please do not discuss the meeting topic during the break amongst yourselves or with any virtual member of the audience. The meeting will reconvene in ten minutes or so, at 3:30 p.m. We're a little bit ahead of schedule here and, is that correct? I'm just going to check with my FDA colleagues that our timing is right. We'll reconvene at 3:30 p.m. Is that right, Letise?

Ms. Williams: Hi, yes. Letise Williams. It is about to be 3:20. So, yes, in ten minutes we can all reconvene here back at 3:30 p.m. Enjoy your ten-minute break.

Dr. Roy: Thanks, everybody.

Committee Discussion of FDA's Questions

Dr. Roy: It is now 3:30 p.m., and I'd like to resume this Committee meeting. At this time, let us focus our discussion on questions from the FDA. Committee members, copies of the questions are included in the materials you were previously provided. I would ask that each Committee member identify him, her or themselves each time he or

she speaks to facilitate the transcription. I would also like to remind members of the Committee that this meeting is classified as a Particular Matter of General Applicability because the matter to be discussed by the Committee is a particular matter that is focused on the interests of a discrete and identifiable class of persons, but does not involve specific parties or products. I'd like to remind public observers at this meeting that while this meeting is open for public observation, public attendees may not participate except at the specific request of the Committee Chair. At this time, I'd like to ask FDA to please read the questions.

CDR Olele: Commander Chinyelum Olele for FDA.

Dr. Roy: Thank you.

CDR Olele: Question 1. Improving informed consent practices may increase the likelihood that patients clearly understand informed consent materials, including the key information and all other aspects of the informed consent for clinical studies, before they or their family members decide to participate. Informed consent forms and the discussions that occur with the healthcare provider prior to signing the form contain various key elements, including the purpose of the study, risks and benefits of participation, and the steps that will occur at the end of the study. A. What do you believe are most— What do you believe are important elements, sections, to include in the key information of the informed consent form?

Dr. Roy: Thank you. We will now move to the discussion in answering this question. And so, please, Committee members, raise your hand, and I can call on you and we'll take the comments down. So, any comments from the Committee?

Ms. Williams: Hi, Dr. Roy. This is Letise Williams, FDA speaking. Do you— Can you not see their hands raised?

Dr. Roy: Oh, I can now see. I see one hand raised, so I see— Thank you, Letise. I see Necie Edwards. Necie.

Ms. Edwards: Hi. Necie Edwards. I think the others were before me, who had their hands raised.

Dr. Roy: Thank you, Necie. Yes. I now see there was a bar going across my screen. Apologies for that. So, I do not know who was first, but I'm just going to start across my screen. So, I'll start with Terri Diaz.

Ms. Diaz: Thank you. Terri Diaz. So, I think that the most important thing that we've heard today was about the point of contact and who to go to if they have questions. So, I really feel like that would be an important element to make sure that it's on the informed consent.

Dr. Roy: Thank you, Terri. Next. Camille Nebeker.

Dr. Nebeker: Camille Nebeker. I think my concern about the key elements is that we're building what we think of as informed consent on a foundation that requires research literacy. And if we don't take the time to develop the research literacy and help people understand the difference between participation in research and informed consent in that context, an informed consent in the context of receiving healthcare, I don't know that we will achieve an informed participant, regardless of what key elements we present in a consent form. So, I think that my concern is that we're not taking the time needed to develop capacity among those who would be involved in decision-making.

Dr. Roy: Thank you. Next is Elizabeth.

Dr. Joniak-Grant: Thank you. Elizabeth Joniak-Grant. I think I want to echo the point about the point of contact. I think that is really significant. It's something that's often on a last page or buried deeply. And it's something that should be up front. I think the— A lot of people expressed that they really want risks outlined quite well, and

obligations as well. I think having that risk information— And this could be something that could go later in the document. We can debate if it's key or not, but I think having that importance of contact is really— It's something that's critical for people to really understand, and the obligations, I think, with aftercare. I think so many times there's not— There's consideration of immediate threat to physical health, but not financial responsibilities, not how does that impact insurance? If I have this device and the study ends, who do I go to see if my doctors don't know how to work with this device? So really outlining— Having some idea of what aftercare might look like I think is pretty critical for just someone making an informed dissent. And there's obviously other things, but I will leave it at that for now. I want other people to have a chance to bring up their pieces as well.

Dr. Roy: Thank you. Adam Berger.

Dr. Berger: Thanks. Adam Berger. I'm going to go immediately off of what Elizabeth just mentioned here, because I do want to push and I think it's coming clearly that we really need a section in the informed consent on those post-trial considerations. I think we've heard that today pretty substantially from a lot of different avenues here. And it's going to have to be fairly substantial in terms of what it's going to address; things like care, you know, the care that's going to be provided afterwards, the cost for that care and who is responsible, the potential risk for adverse events that are going to come up, things around device maintenance, software updates, which hasn't been raised today. But just as a reminder, devices don't run themselves. They actually run off of software. So, there's an entire other component that actually has to be considered here. You know, one thing that hasn't really been discussed is the lifespan of these devices. And what happens when you reach the end of a lifespan or a cycle for that? What is going to occur here, especially if it's a device that's going to be implanted and reside in that individual

for decades to come potentially? Even some of the risks around explantation that we heard today. We heard about issues around what kind of materials are being implanted in addition to the device. We also heard about different considerations around what those risks might be and if those are going to remain as well, you know, if they can't be removed during an explantation procedure. All of those things factor into a concept of really just getting a better understanding of what the post-trial considerations are, because it's essential before you go into a trial that an individual understands the entirety of the risk, not just the risk that's taking place during the study. So, I'll leave it there, but lots more to think about for this area. Thanks.

Dr. Roy: Thank you, Adam. Ian Burkhart.

Mr. Burkhart: Thank you, Dr. Roy. Ian Burkhart here. It's convenient of going right after Adam, because I was going to talk about the end of trial and longevity of devices, which he mentioned on. But I also want to include making sure that a lot of these trials are being done because of unknowns. It's research because we don't know how well these devices or therapeutics are going to affect a certain class of individual. And so, making sure that that is acknowledged, but doing everything that can be done so that direct study risks, the benefits of participation, and what occurs after the study is thought through as much as possible with the lack of having a crystal ball.

Dr. Roy: Thank you. Next. Jijo James.

Dr. James: Thank you so much, Dr. Roy. Jijo James. Again, I think we've had some very comprehensive input in terms of what should be the important elements, starting with Dr. Morales and all the speakers in the morning and what we heard during the Open Public Forum. So, I think we've got a lot of input out there. What I feel we're challenged with is this big issue of balancing comprehensiveness with clarity, and that's something that definitely needs a lot more research, and trying to figure out where we

draw the line and how we slide it. The second thing that I will say is we've got to balance the desire to drive consistency with recognizing the individual differences between disease states, patient populations, etc., as well. So again, as we look at all these elements, at least two things to consider as we prioritize. Thank you.

Dr. Roy: Thank you. Meg Doerr.

Ms. Doerr: Hello. Meg Doerr. I'm very consistent with Jijo's comments just then. I think it is really important for us to think very critically about what is essential to include in each stage of the informed consent process, and to recognize that it is unlikely to be able to accomplish true informed consents in a single interactive experience, whether that's in person or virtual, regardless of the modality. So, understanding, thinking critically about what might be the most essential information to present initially and then walk forward from there might be good. Very much consistent with what we heard during the Public Comment Period about the study that was being done with tetraplegics, you know, having multiple stages, multiple steps in the informed consent process, and obviously for emergency situations. That might be something that— What needs to be known during the emergent period and then what needs to be followed up on afterwards.

Dr. Roy: Thank you. Dave White.

Mr. White: Thank you, Dr. Roy. This is Dave White. One key information that I would like to see included is, speaking as a person who has consented to participating in three out of four clinical trials, why I am being asked if I'm interested in participating. Emphasis on the word I, the personal aspect. And I say that because the one time that I did not— The conversation didn't even get to a consent discussion because the person who was asking me wasn't prepared to answer that question. So that's why I wanted to mention that, and also say that I think that aligns with Dr. Tarver's remarks when she

said that people need to know why they are raising their hand, and also aligns with some of Mr. Merritt's comments as well.

Dr. Roy: Thank you. Necie Edwards.

Ms. Edwards: Thank you. This is Necie Edwards. And a couple of things that— Everything is discussed by the Committee I agree. It's vitally important, but what I want to add to that is also, as someone with a chronic illness, the impact on standard of care. I would like to know if my participation is going to alter my current medical care, if certain treatments may be withheld, or if there are additional expectations beyond the standard of care. I've been in situations in a trial where a lot of this was not fleshed out, it was not transparent. And then, the other thing is that I want to know more about the contact information for questions or concerns. It was mentioned earlier by someone. What happens if you move or relocate? To make certain that all that is clear, you know, provide that contact information for the study team, the clinical research coordinator, the principal investigator, patient advocate, or the IRB. Thank you.

Dr. Roy: Thank you. Are there more comments from the Committee? Am I missing anybody's hand?

Ms. Doerr: I just had one more comment.

Dr. Roy: Thank you.

Ms. Doerr: Yeah. Hi. This is Meg Doerr again. One other thought that I had that I neglected to share was that— We really heard during the— From the report-outs on the Breakout Sessions about different people's needs for different amounts of information, and creating systems of informed consent that allow for information seekers to have their thirst quenched and for people who are less information-seeking to not be overwhelmed by the tsunami of information that might be available. I think that

dynamic information-giving is something that also might be a step forward in our informed consent practices.

Dr. Roy: Thank you. So, at this time, I'm going to provide a summary of these comments for Question 1, and what I heard here. So, to the FDA, with regard to Question 1, what we're hearing is that the Committee generally believes that some of the most important things to consider here are identifying a point of contact within the clinical trial. And the— And again, I'm just going to go through and summarize some of these. I'm just getting a message. Did I make sure that everybody got their points? And I'm sorry, Elizabeth, I see your hand up. So, before I go into my summary here, I'd like for you to have a chance to comment as well. So, please go ahead.

Dr. Joniak-Grant: Thank you so much. I— Yeah. I wanted to make a comment on this idea— Elizabeth Joniak-Grant, sorry. I wanted to make a comment on this idea of dynamic information-sharing, and it harkens back to some comments that were made earlier. I think these ideas are really great. I think where we run into issues is that really doing a patient-centered informed consent— Right? Is that IRBs, and so much of how the structure has always been, is that it has to be the same. It has to be uniform. There can't be any variation. And so, you know, to answer some of the questions of why do things persist, even though we have good data that suggests that things should be done differently when it comes to informed consent?, I can speak to that a little bit because I am a researcher and I am a patient, so I've seen both sides of it. I think a lot of it is that, you know— Every person on an IRB generally wants to have some input onto what's included. Individuals on a lot of IRBs— It can be volunteer at times. They're not always up to date on what are best practices. Researchers are under time crunches, trying to get things through and not having multiple revise and resubmit, revise and resubmit. I mean, we've had to provide journal articles where we're like, “This is the accepted

practice of how to do compensation in a way that respects our participants." And the IRBs don't have that information. So, I think one thing we have to be mindful of in our discussion when we talk about what would be key information, what would be the pieces? is how do we get the IRBs on board with allowing these recommendations to proceed and what that might look like? And so, I just kind of wanted to draw our attention to that for a moment and maybe hear what some of the other Committee members have, or just keep it in the back of our heads as we move through. But I think we can't do these other pieces without this piece falling into place as well.

Dr. Roy: Thank you. So, just in terms of comments, as they relate to responding to the question— Camille, a comment from you.

Dr. Nebeker: It's a really important point. And, as it was mentioned earlier, IRBs use templates to guide how informed consent looks and it doesn't allow for creativity or wiggle room. And our regulations just say, "Here are the eight things that need to be in there." How you go about conveying it should really be appropriate for the population that you're planning to engage with. I've seen IRB-approved consent forms that look like every other consent form, going with a researcher to the villages in Guatemala, where I absolutely know that that's not the consent form that's going to get delivered because the researchers know that this isn't appropriate for my population. And so, it invites a compliance issue because the researchers want to engage with people who they would like to invite in their studies, but they have to use this template. And so, I think sponsors have an incredibly important role here. So, if they allowed or required in a budget or in a proposal time to build the relationships that are needed to engage with community members, to get feedback on the design, the consent communications, how consent should happen, what stages it should happen in over time, there's so much that needs to happen that needs to be driven by sponsors of research. And then those

sponsors, it trickles down to the institution and the Institutional Review Boards and to the researchers and then to the participants. So, I'm thinking about an ecosystem of ecological behavioral model where we look to see where in this model are the touch points where we can affect change. So, I think, the system is a really important piece, and thank you, Elizabeth, for bringing that up, because without having the system in place that can support change, the change will not happen. And that's why I think— When Dr. Kass was speaking, she said it's broken. And if we keep coming up with ideas of how to fix the consent form, that's not getting at why it's not working. Thank you.

Dr. Roy: Thank you.

Ms. Doerr: I would add quickly to Camille's point. This is Meg Doerr. Not only are we facing the requirements of various regulatory— Various IRB boards, but also, the language suggested by many legal departments. And so that can really force the hand of researchers. It can force the hand of IRBs to include language that is in the best interest, perhaps, of the institution or device sponsor, but not necessarily in the best interest of the informing process for the participant themselves. So, I think we need to recognize that additional party within the process of identifying what belongs in an informed consent and what deserves highest priority.

Dr. Roy: Thank you. Adam.

Dr. Berger: I just wanted— Sorry. Adam Berger. I just wanted to respond a little bit to what Camille was saying because it's a really important point about engagement and it's something we take seriously at NIH in terms of how we're actually thinking about this. So, as a sponsor, I'll make a little comment here. We actually launched an initiative to try and get a better handle on how to do this. And that initiative is called the “engage initiative,” specifically meant to develop a framework for engagement.

How do we bring research participants truly into the process of development of our studies, thinking about full engagement from design? What are the outcomes that we are going to be measuring all the way through to how we're actually implementing these? I think that is the broader concept that we're really thinking about how to do this in a more systematic approach. So, we can really have this help improve the clinical research enterprise to address— So, I don't want to go further into that just because I'm not looking to advertise necessarily. But I just wanted to note it's something we have recognized in our taking steps to try and address. But I do think if we— If I bring back, because I think Rob actually mentioned it in his recorded remarks, we do need research on how to actually think about what is the best means for actually meaningfully informing individuals.

And I think that is largely a question here, and maybe that's the real crux of what Elizabeth is trying to get at. How do we actually do this in a way that's going to actually really be impactful for research participants, not just meeting the regulatory requirements? I think it is a question that does need a lot more research when you think about how to implement these, but you know, there are some best practices out there, and I think some of this is really about thinking how we actually can move towards the implementation stage. I know— If we think about what Neal Dickert had mentioned, he specifically talked about some of the differences between the work that he did with IRBs, you know, multi-site research, doing this across multiple IRBs, where they're all trying to provide input into an informed consent versus the success that he was mentioning from a single IRB standpoint where he got deep engagement. I mean, it is a successful engagement. I think he called it “collaborative,” if I remember what he specifically said. There might be pieces there for us to be thoughtful of as we move forward in terms of different types of changes.

I probably don't need to tell this group the Common Rule— 2018 revisions to the Common Rule put into effect the cooperative research provision, which requires multi-site research to actually be conducted under a single IRB. So, there are opportunities to think about how you use the current regulations to help enhance, maybe, the way that an informed consent is actually being developed. I've talked for a while, so I'll stop, but I think there are some different mechanisms that might be useful in thinking about how to move forward here.

Dr. Roy: Thank you, Adam. This has just been such a robust and rich conversation. I'm going to do my best to try to summarize it now, unless there's anyone else that's got another comment before I bring Question 1 to a conclusion here. Just make sure I'm not missing anybody.

So, I started out by saying this is our summarized commentary to the FDA with regard to Question 1. I would say that the Committee generally believes, and I'm going to use one particular Committee member's points here, that there are some dichotomies in the way that we are thinking about, looking at the challenges with informed consent. There's the issue of the comprehensive nature of what needs to be conveyed to patients, coupled with the need for clarity. And that brings us into a lot of discussion points there around what is comprehensive, how much information to give. There's a dynamic range of information-seeking amongst patients. There's also issues around health literacy for diverse patient bases. So, that comprehensive nature of what it is that needs to be conveyed is something to think about when we are marrying that with our desire to make it clear and more simple for most people to digest and to understand, and particularly, as we've talked about at an eighth-grade level.

Some of the concerns that come up along the comprehensive nature of what needs to be conveyed in the informed consent build around, I've started out by saying,

identifying a point of contact, not just for the current trial scenario, but for what happens post-trial. So, looking at, you know— What are the obligations for patients once they are— When they are in the trial, but then when they are completed with the trial? And what are the obligations of the study group to the participants who are in the trial? So, I'm just looking at this globally around the comprehensive nature of the information that we provide in an informed consent, marrying that with clarity on it. So, we've talked about making the information more simplified, where we are clearly stating to patients the risk-benefit of participating. What is the context of those risks in the context of their healthcare delivery? So, what does that look like? And making that clear to participants.

We've also thought about, and again I'm going to use another Committee member's words here, what has been described as a tension between consistency in what we are delivering in an informed consent versus what are the individualized needs of folks? And thank you, Jijo, for these comments that I'm using to bucket some of the more specific commentary here.

And when we think about the consistency of how we turn out informed consent, I think that really brings up some of the topics that we talked about at the end there with the ecosystem around delivery of informed consent. So, if we want to make these changes in how we do better or we use best practices or we make the informed consent process better for patients, how do we do that in a consistent way while taking into account legal, other kinds of compliance issues or other ecosystem challenges that mandate the kinds of information that needs to be included in an informed consent and then marrying that with how does that affect individuals? So, there's individualized needs that folks have as they come into a trial. And so, I think that pretty much summarizes what I have heard here.

One final thought process that the Committee has concerns about is the post-trial considerations and making sure that patients can understand— Have a way to understand or have a way to access what it means to them in their ongoing healthcare scenario once they are completed with the trial, if there's something that's implanted in them or some type of device that is going to need maintenance, software updating. What is the lifespan of that device? And what do you do if your healthcare provider doesn't know about this new device that has come to market? So, how does that impact the long-term care for the patient? And again, what are the obligations that we have in terms of telling the patient what they are going to need to do and explaining to the patient what their obligations are going to be long term in terms of managing what it is that they have undergone in their trial, whether that be an implantable device or wearable device or software concerns there? Where do they get the information? Where is their point of contact? What's the ongoing maintenance scenario for the patients?

I think I've summarized some of the major points that are here. So, I would ask to the FDA, is this an adequate summary of our discussion to Question 1? And to Commander Olele?

CDR Olele: Yes. I will turn it over to Dr. Grossman.

Dr. Grossman: Thank you so much. Thank you, Dr. Roy. Yes. This is an adequate, highly adequate, discussion and points of consideration, and we don't have any clarifying questions to ask.

Dr. Roy: Okay. Thank you. So, with that, we'll move to Question 2.

CDR Olele: Chinyelum Olele for FDA. Question 2. How could the contents of the key information be presented to help you decide whether to participate in a clinical study? Please consider the following in your response and how they factor into your decision about whether to participate in a clinical study: Order in which information of

the clinical study is presented; accessibility of the informed consent form (i.e., language, literacy, considerations for physical or cognitive differences, etc.); other health equity and cultural considerations.

Dr. Roy: Thank you. So, now we'll go into a discussion for Question 2 and I invite Committee members to raise your hand and I'll call on you as I see. Thank you. We'll start with Elizabeth.

Dr. Joniak-Grant: Thank you. Elizabeth Joniak-Grant. I think, to me, again, these are the questions, like the hows, the whos, the whens. I think it's really important to emphasize this idea of a bullet point or summary sheet where you can get a quick overview of what's going on with informed consent and to have the informed consent be, perhaps, in chunks, right? Like, you can move through it with somebody section by section, instead of these long blocks of text for the written. But what I really want to draw attention to in this moment too, is this idea of informed consent as a process. It was mentioned quite a few times, I think a lot of times, that informed consent is seen as the single moment. And so, I think this idea of having some pre-consent information go out, sort of what is this study? You know, overview some of— A big overview of some of the risks and benefits, and then asking the potential participant, “Would you like more information?” And potentially saying, “How would you like the information?” I think one way that we really can work with participants is to recognize that some people, especially if we're talking about people with illnesses, right? They have particular ways that they learn better than other ways. And so, some people might want to sit down and read, some people might really want that video information. Some types might be more culturally-sensitive, where your family might be a part of making— Of the decision making, where you'd be watching a video altogether. And so, I think trying

to think of ways that we can put a little bit of the power of how that information is given into the hands of the potential participants could be really beneficial.

Along with that, I think the timing is really important. You know, people have brain fog. They have good days; they have bad days They have just chaos that's maybe happening if they're in the middle of, you know— Me recently bringing my child in for a pre-op appointment, they were suddenly with the anesthesiologists and all the other people in the room going, “So, do you want to be a part of this study?” And I'm trying to keep my kid calm. I'm trying to focus on everything else that's going on. And that just felt like complete overload to try and manage that. So, I think being really mindful of what good timing looks like, what gives people the space to think about things and ask questions, and have time for reflection, and where they don't feel compelled to make a decision on the spot. And along with that is this idea of where consent happens, right? Like, is it a separate office? Can you have someone sit with, or if there's a child involved, sit with the child for a minute? Or if it's for you and you just can't balance everything. Would they want to meet at a library and go over things? Would it be better to do it by video if they're quite a distance away? So, I think giving participants more say in when and where consent happens would be really beneficial for giving them at least the room to start processing through all the important pieces.

And then, one final thing. I did want to mention there’s a lot of talk about video and such. The importance of maybe having subtitles involved with video presentations for hearing difficulties, any type of processing issues. And that could also help with certain types of multiple languages, and clarification would be beneficial as well.

Dr. Roy: Thank you, Elizabeth. I believe, Ian, your hand was next.

Mr. Burkhart: Thank you. Ian Burkhart. I think, going first, the order of how the information is presented is very critical. If you lead off with all the risk, especially if

you're talking about a surgical procedure for an implanted medical device, one of those risks is you could die. If you lead off the bat with that right away, that can really skew someone's perception and potentially shut them down on listening to other information. And so that order needs to really be considered, as far as how it's being presented, between the risks, the what's being done, the why it's being done, the potential benefit.

One thing that we haven't really talked about today is potential compensation for individuals that participate in these trials and how that can skew things as well, whether it be an enticement for people to participate or it be more of a deterrent because then, if they're already on disability or other social forms of assistance. But really just getting the information into multiple formats, I think, is something that's been echoed quite a bit today. And because everyone learns a little bit differently, everyone's going to process the information a little bit differently, and making sure that there's that open dialogue that the potential participant feels comfortable enough to ask questions and doesn't feel that, “Oh well, I should already know this, so I'm not going to ask” or “They're going to think it's a stupid question, so I'm not going to ask.” But really make sure it's a level playing field and that there's enough of a rapport between whoever it is that's presenting the information to the potential participant, and then going back the other way as well. Thank you.

Dr. Roy: Thank you, Ian. Next. Terri.

Ms. Diaz: Thank you. Terri Diaz. I agree completely with what Elizabeth and Ian just said. They made a lot of good points of what I was going to say, but one of the things that I thought of was, if it's a long-term study and there are different times of informed consent, in the beginning of the study, there would be a stage one and then in the middle of the study, maybe stage two. And at the end, that way the information isn't an overload of informed consent all at once, something like that. And then, visuals. I

think that visuals and what— I don't remember who said it, but somebody who really wants to read a lot of information has all of the informed consent and someone that just needs the bullet points.

Dr. Roy: Thank you. Next was Jijo.

Dr. James: [Indiscernible – 03:12:58 - 03:13:00] I think we've got some really good input in the morning from my co-panelists. I'd like to focus again on a public process and make three points.

Number one: As we think about technology and using technology, let's also be mindful about the health equity and cultural considerations and not inadvertently block somebody out or exclude somebody because of challenges with digital literacy, etc. So, not a showstopper, but something to consider to ensure that we're being inclusive.

The second: As we think about modalities of communicating this information, be it pictorial videos, different formats, I just draw what we spoke about for the previous question and draw attention to the fact that we will be increasing IRB workloads. We need to be aware of that and try and help balance some of that as well, and figure out if there are more efficient ways of doing it. We've got technology available today. Can we stand a template for some of these? Can we figure out what sections are needed based on the kind of study that you're doing? Do we need to really reinvent the wheel? Is there an opportunity out there?

The third point that I'll leave you with is: I really like the idea of checklists that were mentioned because I see checklists not as a list, but as an opportunity to invite a conversation. If you look at what has been done with the Safe Surgery Checklist that's used globally or the Device Briefing Tool, it's not the questions out there, but the conversation that happens. Is there an opportunity to have a conversation at the point of care before the patient participates in the trial? Are you aware of participating in a trial?

Have you been consented through the process? Do you know everything that you need to know? Do you have any questions? Are you ready to start? I mean, simple questions. I'm sure we can research this, but simple, generic questions that invite a conversation that hopefully gets us over some of these barriers that we have around getting standardized language, etc. We can do all of that for the legalese and the regulatory requirements. This enables that conversation and something that we should encourage. Thank you.

Dr. Roy: Thank you. Meg.

Ms. Doerr: Meg Doerr. Again, building from Jijo's point, I have often spoken about informed consent where much of the experience can be unknowable in advance of participation as being very similar to other contracts that we agree to that have large unknown components, for example, marriage. Right? When we agree to be married, there's no way for us to know about what's coming next, like, will the socks be left in the middle of the living room floor? You know, will our partner never recap the toothpaste? But we know who we need to be in dialogue with, and also the standard nature of the contract. That rhythm of marital vows helps us know what we're getting into, whether we're in a drive-by— Drive-through place in Las Vegas, or whether we're standing in front of our faith congregation or whether we're in the office of the Justice of the Peace. And so, I think that there are lessons that we can bring across to the informed consent process about creating some amount of standardization, but also recognizing that there is no way to convey all of the information in one instance, that this is an ongoing dialogic contract that we're entering into that requires continuous communication.

Dr. Roy: Thank you. Camille.

Dr. Nebeker: Camille Nebeker. I think I just want to add and build on this, but in our prior research, we've worked with older adults, Latino populations, Native Hawaiian, Pacific Islanders. They all bring up different needs and different ways of wanting to get information. And I think just— And I'm so happy to hear what you had to say, Adam, about the work that you're moving toward within the NIH for engagement, because by engaging with the people who we think will be those in the study, we've learned that they want to have town halls; they want to have information shared in a community setting; they want to be able to pick and choose which part of the informed consent they review first. If it involves a technology that's capturing their location, it's going to be really different with certain populations that are concerned about their legality status or where they go in their everyday life. And so, I think just having opportunities and really engaging with populations who you plan to engage, it's just going to be critical because you'll learn different things.

Dr. Roy: Thank you, Camille. Other comments from the Committee? Okay. Seeing none, I will move to give an overview here of our response to Question 2. And so, FDA, with regard to Question 2, the Committee really has a lot of commentary around process, and to borrow words from a Committee member, this has a lot to do with it the who, how, when, what we are looking at with informed consent. A lot of discussion around the process being not just a one and done situation, that informed consent is an ongoing dialogue and discussion with the study and with the study team. Their discussions, in terms of when informed consent is done, physically, when— Where that happens. Does that happen in the care setting? Does it happen in a preclinical scenario? Is that— Does telehealth factor into this? Can it be done that way? What kind of information can be given to patients to learn and in what format can that be done? So, looking at different needs of diverse populations that are coming into a

trial. Is it a town hall? Is it video again? Is it— Are we talking about a video way of delivering that?

So, again, process. We've talked about timing. We've talked about where this happens. We've talked about it being ongoing conversation. And I think the Committee has also had some interesting commentary on addressing the unknowns that patients would have coming into a clinical trial. And again, some of this need to balance standardization around what we do in informed consent. There are needs to doing that for compliance and regulatory, but standardization can give a rhythmicity and cadence to the informed consent process that can actually give some anticipatory comfort to patients as they come into an informed consent. So, we know that there's going to be, "This is what the process is going to look like. You're going to hear from us these times." There's a phased approach, perhaps, to the informed consent process.

And then finally just the Committee also continues to have concerns around the visual interaction of the materials that are being given to patients as they come in, whether that be auditory, written infographics. Is it video? Is there closed captioning on the video? Is it transcribed in multiple languages? Are we being thoughtful about that and making sure that we're not excluding individuals or communities based on cultural needs or other sorts of diversity-based challenges that individuals may have in the community?

Cyndi, to the FDA, is this an adequate summary?

Dr. Grossman: Thank you so much. I was told that I had a little bit of fuzziness on my audio. Can everybody hear me okay?

Dr. Roy: Yes.

Dr. Grossman: Yes. Okay, great. So, we do have actually a clarifying question, and I just want to frame it for a minute and then I'll ask the Committee. The frame is

really around the ways in which to think about the order of information that would be presented and what, maybe, top— Rises to the top of that order, thinking about maybe what are the first few things or the first three things that folks would want to see? And does that change based on a population that would be participating in the research or the level of risk of the research intervention, for example, whether it was something that was not implanted or implanted, for example? So, I'd love to hear a little bit more about that. Thank you.

Dr. Roy: Thank you. I will open that back to the Committee for discussion. Elizabeth.

Dr. Joniak-Grant: Thank you. I think one of the most important pieces in terms of order— One of the first pieces should be, "If you decide to be in this study, this is what's going to happen to you." To just get right to the point because if people aren't comfortable with that piece of it, there really seems to be no necessity to go into all the other pieces. But I would like, you know— This is a discussion I'd like to hear what other people have to say, because I could be completely off base with what I think patients might want.

Dr. Roy: Thank you. Meg.

Ms. Doerr: In specific order of the information to present: This is research. It is voluntary. We are asking you to do blah. We are asking you because you blah. And then risks and benefits. I think that that would be the most critical information from my perspective. And again, I mean, to return to the marriage analogy, that's the nature of the marital contract, right? Like those are the essential things that are incorporated there. Who, what you're agreeing to, why you're agreeing to it, and the fact that it's voluntary and you have recourse.

Dr. Roy: Thank you. Adam.

Dr. Berger: Thanks. Adam Berger. So, I just want to— I think the purpose of the research needs to be front and center, at least as the initial information, before diving into the specifics of what's going to happen to you in it. And I think, reflecting on what Dave White had mentioned before, why is that an important research project for you as the research participant? I think is an essential piece to be able to start with. I think I largely agree with Meg for the rest of the ordering. I just think I would put that at the very top end of this. And there are obviously other pieces of the key information that we haven't spent a lot of time talking about, things like the duration and the procedures that are going to take place, the compensation for medical treatment and research-related injury. The other section we've been putting forward is a new piece for this around post-trial considerations. I mean, I think all of those come after that. But I do think it has to flow from what the purpose is, and then, coming through to the risk that Meg was outlining. Thanks.

Dr. Roy: Thank you. Elizabeth.

Dr. Joniak-Grant: Thank you. Elizabeth Joniak-Grant. I definitely agree with Meg to really highlight that it is research, but to define what that means, because again, that's not really an eighth-grade reading level or less for a lot of people, and that it's voluntary. I would agree with Adam about having the purpose there, but I think what— We have to be very careful because a lot of times when people are doing research studies, they get very committed to giving the purpose in their scientific ease and using very specific terms that are very exact, and so, the purpose of the study gets lost on most people. So, I would say, yes, we could put the purpose further up, but it would have to be in a really easily understandable language for everyone who's participating and not in the exacting language of the research scientists conducting the study.

Ms. Doerr: Building from Elizabeth's point and acknowledging Adam's clarification, my perspective would be that the this-is-why-we're asking-you component of the key information would speak to that purpose. So, we're asking you because you fit into the purpose of this research. So, relating the purpose of the research to the person rather than talking about the purpose of the research in the abstract.

Dr. Roy: Thank you. Jijo.

Dr. James: Thank you, Dr. Roy. Jijo James. So, I agree with everything that Meg, Elizabeth and Adam have said. The only point that I would add is I agree order is important and we can figure that out, but probably equally important to figure out the backstop, right? Understanding. So, we can do it in whatever order. I think it is effective only if we check if there has been comprehension. Does the patient truly understand what they have read? So, I think you need to balance both of those out as you look at this.

Dr. Roy: Thank you. Adam.

Dr. Berger: Thanks. Adam Berger. I just wanted to just second what Elizabeth was saying about ensuring that the language that's used is in an appropriate level, and that can be hard, especially as a scientist. I can say that can be hard for us. But, you know, I think that— I think it gets into the next question a bit, so I'll just do this briefly. This is where I think it's important to make sure that we're taking advantage of the tools that are available, the resources that are out there for helping to create understandable consent language. There are some that are available even through NCI, for instance, on evaluating readability, that kind of points. You've got other tools you can apply to your language. I think it's really essential that we take it upon ourselves to become aware of and help disseminate what those tools are so that others can help take advantage of that and ensure that we're getting to that language that's going to be at the eighth-grade

reading level or below, and preferably as low as possible, so that we aren't— To get to the health equity lens that Jijo was mentioning earlier. And I fully agree with what he was saying before as well. We don't want to exclude people not only because of visual literacy, but also just literacy in general. So, we want to make sure we are making our informed consent language as accessible as possible.

Dr. Roy: Thank you. Camille.

Dr. Nebeker: Camille Nebeker. And just building off of that comment, Adam, about utilizing tools and then thinking about how comprehensive it is versus how accessible it is. We tried taking IRB-approved language for a consent form and running it through a large language model to get it to produce readability at around the fourth-grade reading level. And what happened is a lot of text. It was very concise. It was very concise, and it left out what I thought might be important information. So, we asked participants to compare the IRB version versus the large language model version. And what it did is it prompted a lot of conversation. So, when they didn't get enough information, they started asking questions. So, I think we really have to be thoughtful about do we want to give a lot of information or do we want to engage in conversation and have that bidirectional interaction? So, depending on the goals of informed consent and how we want that to be accomplished, it can either be a lot of text and very comprehensive or it can be snippets that allow for inquiry. So, I think that— It was just a really interesting finding that we came, that we observed in our research.

Dr. Roy: Thank you, Camille. Elizabeth.

Dr. Joniak-Grant: Thank you. Elizabeth Joniak-Grant. Just a very quick point. I think using— Writing in the active voice would be very beneficial, getting out of the journal article passive voice. It has been shown that using active voice can help with comprehension, so just a very quick point.

Dr. Roy: Thank you. Dave White.

Mr. White: Thank you, Dr. Roy. Dave White. I love these comments and this discussion. And I wanted to— I was just thinking. I wanted to say that I propose that what's most important up front is what the person who is contemplating consent thinks is most important. Okay? And I say that because it gives us an opportunity to marry what's important to establish patient-centered informed consent. So, to make that happen, we would have to think of ways of creating a dynamic informed consent form that incorporates the best qualities of what I'm proposing.

Dr. Roy: Interesting. Thank you. Jijo.

Dr. James: Thank you, Dr. Roy. Jijo James. I'll keep this brief. I think the one thing that I also remembered is it needs to— The order is probably going to be situational. I hearkened back to the presentation earlier today by Dr. Neal Dickert, I think, who talked about in an acute care setting, in an emergency setting, if you're looking at doing trials in those settings, the informed consent and the order might look very different. So, you need to be able to adjust it situationally as well.

Dr. Roy: Thank you. And Meg.

Ms. Doerr: I wanted to echo— Meg Doerr. I wanted to echo Dave White's comment about what's most important to the person themselves. This is very consistent with adult learning theory, that people are more receptive to information when they are asking for the information themselves. I know that Kaiser Permanente has experimented with this, creating a self-directed informed consent process that presents a series of tiles, and then, the person consenting can flip over the tiles in the order that they feel is the most important. This is just one innovative approach to allow for this self-directed consumption of information. And again, consistent with adult learning theory, this has been shown to increase comprehension and retention of information.

Dr. Roy: Thank you, Meg. It's really interesting. Okay. I have the honor of summarizing these incredible comments to the FDA. So, Cyndi, I'm going to summarize our comments here on the order question. And I would say that the Committee generally believes that the order of how the informed consent happens is best done if it can be individualized to what the individual user's needs are, and that if there's some way to do interactive or dynamic informed consent, that's an ideal way to do this because different people will have different things that are most important to them as they're coming into this. The areas that would be important to list out would be identifying, getting right to the point of what the research is about and using the most— The easiest language, the clearest language that we can and perhaps using tools that can help us figure out what some of that clean and easy language is to use. And it's not just because of health literacy, but it's also because when patients are coming into a scenario, they quite often - don't feel well. And so, they're— They don't feel good. So, having easy-to-understand language just makes it more clear to patients coming into it.

And that is true from a health equity standpoint, but also from a patient equity standpoint, that patients struggle with that language as well. So, making it clear to patients that this is research, that it is voluntary, that there are risks and benefits, and the order of that to the extent it can be individualized for the participant would be perhaps the best way to approach doing that. And just with that easy language, again, wanting to balance having it be comprehensive but also accessible. So, I just wanted to use that language there.

Cyndi, is this an adequate response for what the question is asking?

Dr. Grossman: It is, and we appreciate the comments and points of clarification.

Dr. Roy: Thank you. We will now move to Question 3.

CDR Olele: Commander Olele for FDA. Question 3. Considering informed consent should be accessible and effective for all potential participants, what do you believe are the most effective approaches to providing information in the informed consent form and through the overall informed consent process? A. How can informed consent be tailored to meet the needs of all populations, including: 1, diverse racial, ethnic, socioeconomic, gender and sexual orientation populations; 2, underserved populations; 3, the full spectrum of age groups (i.e., children and elderly); 4, individuals with physical or cognitive differences. Next slide, please.

B. How can technology (i.e., video, multimedia, computer-based techniques) be leveraged in the development of informed consent materials and process for clinical study? What are important areas to consider in implementing electronic or digital consent in clinical studies?

Dr. Roy: Thank you. I'd like to point out to the Committee that we are at 4:38, and we have until about 4:55 on our agenda, so wrapping up the day here. These are just big questions and topics that we all have lots of things to comment on. So, I want to make sure that we all have the ability to get our comments in here, in these last few minutes as we contemplate this two-part question here, Question 3. So maybe it is easier when you are answering this question if you state specifically which part of the question you are addressing in your comments. That might make it easier for us. So, I'll start with Necie.

Ms. Edwards: Hi. Necie Edwards. I am going to address section number one and number two. So, some thoughts to consider with number one is to make certain that the content is culturally competent. We need to make certain that they are also culturally respectful. It may help to also consult with the community reps to adapt the language and the images and the concepts that rep— I'm sorry, that resonates with that specific cultural and social background.

Other things that came to mind was making certain that gender neutral language is used to respect participants gender and identities, and sexual orientation. I also want to comment on rural populations. So, I believe that is section, if I'm not mistaken, number three. I may be out of order with that. Please forgive me, but I wanted to comment on the rural population because: Number one, for some of these populations, having an e-form, electronic form, is not going to work. So, some type of short or concise paper form will work better for them. Other things to consider is that, since technology and broadband is— Can definitely be a factor, we need to look at collaborating with those trusted local entities, whether it's the community health centers, rural hospitals, churches, synagogues, agricultural, cooperatives, because they usually have established relationships with those communities and also work with community health workers who understand that community's unique needs. Thank you.

Dr. Roy: Thank you. Dave White.

Mr. White: Thank you, Dr. Roy. Dave White. Necie made it very easy for me because she covered most of what I'm going to say, so I'll go through it quickly.

First, you know, data and hard work cost money, so use it sparingly unless you're paying for it. Second, tailored digital tech for the least tech savvy. Just because there are bells and whistles, it doesn't mean you have to use them. Third, be upfront about what and how data will or will not be used and shared. And last, as Necie has said previously, data breaches. What will happen if that happens? And that's it.

Dr. Roy: Thank you. More comments? Elizabeth.

Dr. Joniak-Grant: Thank you. Elizabeth Joniak-Grant. I feel like we're reiterating things a bit, but again, I think it's— If we really want to deal with some health equity issues and things, it's really important that the participants have a say in how they get the information. So, video has a lot of great qualities to it, but one thing we might want

is a way to flag a slide or a portion of the video that goes to the team, so they know that the person has questions for follow up so they're not trying to figure out how to take notes. Having video prerecorded so they're not trying to stream it and dealing with hitches and those types of things, and to help manage any type of connection issues. And also recognizing that most people these days with video, at least as far as I'm concerned— My husband's a software engineer, so I hear about it a lot. Our accessing these things on phones, so while they might be developed on a great computer system and a screen and everybody's looking at it, people are accessing it on their phones, and we have to think about how would that work for people with vision issues or sound quality, and what would that look like? Giving people the option if they still want it on a piece of paper, and that's how they best process, that they can get that information, or the video transcribed on a piece of paper or PowerPoint presentations and handouts, and things like that I think could be really beneficial. And having multiple languages. Making the digital tech available, maybe in an office. I can meet you or I can meet you at the library. We can go over this together. I can answer your questions. We can look at it on the screen. And just helping with accessibility that way.

I also wanted to speak to number three, the full spectrum of age groups. I think it's really important that we be mindful of assent, as has been brought up, whether it's because of cognitive differences or certain medications people are on or injuries or age group. I think we really have to be mindful that people still should have some say in their body, at least what happens and what doesn't happen. And the idea of just going straight to the person who can give legal consent and ignoring the actual participant in the room is something that really needs to not happen anymore. And, you know, figuring out what would be age-appropriate or cognitive-appropriate, short presentations

of “This is what we want to do for the study. Are you okay with that?”, would be important for working with true patient-centered care.

Dr. Roy: Thank you. Ian.

Mr. Burkhart: This is Ian Burkhart. My comment is— I have two comments actually. One is related to section four. As someone with limited hand dexterity from my spinal cord injury, I would definitely not prefer that someone hands me a brochure or a piece of paper because I can't thumb through it and look through those pages. So, making sure that you're looking at your potential inclusion criteria and tailoring the information towards those individuals I think is really important. And, like has been mentioned multiple times and I think it's a very important fact, it's just everyone processes information really differently so you need to have multiple avenues of this information so that way it can be best understood. And then my second comment is for section one. And it's more so talking about the root cause of who can even participate in some clinical trials, which may be outside of the scope of this conversation, but being able to present to individuals that may qualify for this study and ask them if there are any barriers that might be in the way of them participating and seeing what can be done from the research team to be able to mitigate some of those barriers so that overall, there is more diversity in research.

Dr. Roy: Thank you, Ian. Adam.

Dr. Berger: Adam Berger. I’m going to make this quick. I just want to comment on one aspect of assent that hasn't been discussed yet, and that's largely what happens when that individual turns legal age of majority. If you're talking about— Generally, we're talking about assent for individuals that are under the age of 18 and need to be thoughtful about potentially seeking consent for that individual or from that individual

once they actually reach that legal age of majority. So, this is another consideration to take into account when you're thinking about informed consent.

Dr. Roy: Thank you. Other comments? Terri, did I see your hand up? No. No, maybe— No. Okay. Okay. So, seeing as there are no further comments, I'm going to try to encapsulate what we've talked about here. So, for the FDA, with regard to Question 3 and the many components of Question 3, the Committee is concerned about really accessibility of the informed consent in many dimensions of accessibility. So, there's accessibility from the standpoint of individuals with handicap, and looking at inclusion criteria there and being able to provide numerous pathways for participation, whether that is electronic and, within electronic, is it optimized for handheld devices, desktop devices? Making sure that we take that into account. And then, are there paper options?

And that relates again to the— Not just that— This is handicap accessibility, but then looking at rural accessibility. We know we have bandwidth issues across our nation. And so, how do we address that? The Committee has talked about partnering with trusted community centers, whether that be places of worship or local libraries or other kinds of trusted community centers, to improve accessibility for rural participants.

We've talked about accessibility from a cultural competency standpoint, ensuring that language and imagery resonates with multiple cultures and ethnicities and gender orientation, sexual orientation.

And then finally, we've talked about accessibility from the standpoint of making sure that we've addressed multiple age groups. So, there are different needs of older individuals and different needs of younger age groups, and looking at what is age appropriate in the accessibility of content there, and including the concerns around assent and particularly for pediatric patients who then perhaps during the study are

going to reach legal age. And how are those— How are the assent issues best managed there?

The Committee also had some commentary around clinical trial recruitment and potentially an opportunity to do some education just up front in that recruitment phase that gets in a little bit to this concept of accessibility as well, so that people can know what they might be interested in getting involved in in the ways that they may be able to participate, if they are interested. So, a little bit outside of the scope of the question, but I do think that that was an interesting comment within the Committee.

And then finally, the Committee had concerns about data management. How is data handled? There's the anonymity of data, but then there are questions around do patients have the ability to access their data? So, there are those sorts of questions about data. And then there are questions about data breaches and what happens with it, you know, when a data breach happens and that we make sure that that is something— Data management is a component of the informed consent.

So, I think, to the FDA, I believe I've summarized as best I could the comments here. Is this an adequate response for your needs?

Dr. Grossman: Thank you, Dr. Roy. We do have one specific clarifying comment or clarifying question around a sentence. I'll hand it over to Dr. George Van Hare.

Dr. Roy: Thank you.

Dr. Van Hare: Thanks. Yeah. Just to clarify, because I know the question of assent has come up a few times during the meeting, and we didn't provide any materials specific about protection of children in research to the Committee, but just to comment that the safeguards for children are part of the regulations in 21 CFR Part 50. The interesting thing about assent is that there's a lot of flexibility. Children are required to give assent if they are developmentally capable of doing so, and that assent can actually be verbal

or can be written. And the assent form often is encouraged to be quite flexible and to incorporate things like cartoons and videos and things like that to be culturally and developmentally appropriate for the children. So, there are those regulations, and FDA has published a draft guidance in 2022 covering protection of children in research.

Dr. Grossman: Thank you, Dr. Van Hare. So, the clarifying question was just around the statement, the comment made about young people being ignored in research, and we just wanted to see if the Committee had anything else to add around that particular question or statement.

Dr. Roy: Thank you, Cyndi. Elizabeth.

Dr. Joniak-Grant: Thank you. Elizabeth Joniak-Grant. I think what's tricky there with the guidance is that what does it mean to be developmentally capable? Right? Some studies take that as you have to understand every piece of this as a 35-year-old with knowledge would understand and science background. And then they're developmentally capable. So, at least in some of my experiences, it's, you know— A six-year-old or a seven-year-old can understand what it is to have more blood taken or more tests done and things like that, but they're not necessarily treated as developmentally capable to give any type of assent. And I'm thinking that maybe we should think about and they can only assent to certain pieces of it, but that maybe what it means to be developmentally capable and what that looks like needs to be more clearly defined, because right now it feels like it's very easy to slip out of it, if someone wants to.

Dr. Roy: Thank you, Elizabeth. Other comments? FDA, is this adequate? Cyndi, are there more questions?

Dr. Grossman: Right. Just double checking with my colleagues. There are no more questions for us. I think this was very clear and we appreciate the commentary and the clarifying— The response to the clarifying questions.

Closing Remarks

Dr. Roy: Thank you. It is 4:55 and we are right on time. So, I'm going to move to closing remarks now. I'd like to thank the Committee and the FDA for your contributions. I'd like to thank again the Open Public Hearing speakers, the patient, industry, healthcare provider, academia and FDA for their remarks today. It's been a phenomenal day. And as we move to adjourning, I'd like to ask the FDA representatives if they have any concluding remarks, that is Drs. Grossman, Van Hare, Viviano and Ms. Meeker-O'Connell?

Dr. Grossman: So, I think we just want to thank you so much for your time, for your service and for serving on this Patient Engagement Advisory Committee. As you heard from Dr. Tarver's remarks, that we take these discussions and these recommendations that you put forward very seriously and we take action upon them, and we look forward to being able to report back to the Patient Advisory— Engagement Advisory Committee next time in terms of our progress and action steps. And so, I just really want to thank you for your depth of experience, for your knowledge, for sharing your commentary, and for your time and attention for today's meeting. And a special thank you, Dr. Roy, to you for serving as Interim Chair and for expertly leading us through the day.

Adjournment

Dr. Roy: Thank you, Cyndi. Thank you all. Thank you everybody for joining us at the Patient Engagement Advisory Committee where we, the patients and care partners

provide our perspective to FDA's Center for Devices and Radiological Health. Your participation and the discussion of the Committee today are an important step forward in helping to assure the needs and experiences of patients are included as part of the FDA's approach to improving Patient-Centered Informed Consent in Clinical Study of FDA-Regulated Medical Products. The Advisory Committee Meeting is now adjourned.