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UNITED STATES FOOD & DRUG ADMINISTRATION

Public Meeting on CDER Standard Core Sets: Clinical
Outcome Assessments and Endpoints Pilot Grant Program

DATE: Thursday, December 5, 2019
TIME: 8:34 a.m.
LOCATION: Center for Drug Evaluation and Research
FDA Great Room, Building 31
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
REPORTED BY: Michael Farkas, Notary Public
JOB No.: 3661267

1 P A R T I C I P A N T S

2 Meena Savani

3 Robyn Bent

4 Kanecia Zimmerman

5 Richard Lipton

6 Sara Shaunfield

7 Heather Benz

8 Katie Golden

9 Laura Lee Johnson

10 Elektra Papadopoulos

11 Devin Peipert

12 Michelle Tarver

13 R.J. Wirth

14 Kanecia Zimmerman

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P R O C E E D I N G S

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2 MEENA SAVANI: All right, we're going
3 to go ahead and get started. Welcome to everyone who
4 joined us today. Before we officially kick things
5 off, just our standard disclaimer language. Friendly
6 reminder that the views expressed in the following
7 presentations are not necessarily those of the
8 individual speakers and do not represent an official
9 FDA position.

10 And now, the warm and friendly welcome.
11 Good morning, everyone. My name is Meena Savani. I'm
12 with CDER's Patient-Focused Drug Development staff
13 within the Office of the CDER Director here at FDA.
14 And I'd like to welcome everyone to this morning's
15 public meeting to support the -- for CDER's pilot
16 grant program, which FDA developed to support the
17 development of publicly available core sets of
18 clinical outcome assessments and the related
19 endpoints.

20 We appreciate everyone who's joining us
21 in the room here in person. We also have a number of
22 folks who are joining us through the webcast. So

1 welcome to them as well and thank you to all of you
2 for being a part of this meeting.

3 During today's meeting, just as a quick
4 overview, Robyn Bent from the FDA will provide an
5 overview of the grant's program, specifically the
6 background, the purpose, and the cooperative agreement
7 structure. We will then have a presentation from each
8 one of our grantees who are funded under this grant
9 program, and they'll share their development plans,
10 specifically in the areas of migraine, physical
11 function, and acute pain in infants and young
12 children. We're then going to kind of round out the
13 day with a panel discussion with panelists from FDA,
14 each one of the grantee teams, as well as a patient
15 representative.

16 Following each one of the grantee
17 presentations, as well as the panel discussion, we
18 will have an opportunity for audience members to
19 express any comments or questions to -- and you can
20 direct yourselves to one of the microphones on both
21 sides of the tables. And if there is time, we will
22 also be entertaining questions through the webcast.

1 Before we get started, just wanted to also remind
2 everyone that we encourage you to submit any comments
3 or questions also to our public docket.

4 And a few housekeeping items before I
5 turn the mic over to Robyn. A recording of this
6 meeting and transcript will be available and archived
7 on our public website. We do have a 15-minute break
8 scheduled around 9:45. But if you do need to step
9 outside to stretch or to grab a quick snack at the
10 kiosk, we welcome you to do so throughout the meeting,
11 and we do plan to wrap up around noon.

12 And there is also a kiosk, if you
13 didn't see it yet, right out here in the hallway in
14 the main lobby where you can also grab snacks or
15 beverages. Bathrooms are down the hall. So if you go
16 out here, make a right, you'll see them on your left
17 at the end of the hallway. And if you're looking for
18 internet access, the Wi-Fi password was on the first
19 slide. But if you didn't catch it, there's also a
20 sign right outside at the front lobby that you can use
21 to get the password.

22 I would now like to introduce Robyn

1 Bent to the podium for her presentation. Thank you.

2 ROBYN BENT: All right. Thank you,
3 Meena. Good morning, everyone. I am Robyn Bent. I'm
4 the Director of the CDER Patient-Focused Drug
5 Development Program and the FDA Program Officer for
6 the Standard Core Clinical Outcome Assessments and
7 their Related Endpoints Pilot Grant Program. I think
8 we're going to need to work on a slightly shorter
9 name.

10 I want to start by saying how much we
11 really appreciate you being here today. The goal of
12 this meeting is to hear from stakeholders, both during
13 the question and answer period, as well as in the
14 public docket so that these standard core sets of
15 clinical outcome assessments are developed, the
16 identified concept COAs and endpoints reflect what is
17 most important and relevant to patients, and support
18 regulatory and potentially other stakeholder decision
19 making.

20 This program only started this fall, so
21 we're still early in the process. This meeting is
22 really going to focus a bit more on what we're

1 planning to do than on what we've done, and we plan to
2 have meetings twice a year to get feedback. And we
3 anticipate that in the future, there'll be much more
4 opportunity for stakeholders to review deliverables
5 and provide that feedback.

6 So I'm happy today to provide you with
7 a high-level overview of the grant program, why FDA
8 felt it's needed, how it's currently structured, and
9 what we hope to accomplish.

10 I'm going to start with a little
11 history. Back in 2013, the FDA started holding
12 disease-specific public meetings that strengthened our
13 understanding of disease and treatment burden. These
14 were our patient-focused drug development meetings,
15 and we realized that these meetings provided an
16 important opportunity to hear directly from patients,
17 patient advocates and caregivers about the symptoms
18 that matter most to them, the impact the disease has
19 on patients' daily lives, and patients' experiences
20 with currently available treatments.

21 These meetings reinforced that patients
22 with chronic serious disease and their caregivers

1 really are the experts on what it's like to live with
2 their condition. We learned that the chief complaints
3 heard in PFDD meetings were often being factored
4 explicitly into drug development plans, and that often
5 they weren't being measured in clinical trials.

6 We also heard that patients want to be
7 as active as possible in the work to develop and
8 evaluate new treatments. So building on what we
9 learned and continue to learn from those meetings,
10 we're looking ahead to enhancing incorporation of
11 patient input into drug development and evaluation.

12 This will bring us to our vision for
13 incorporating patient input as standard practice: We
14 want to ensure confidence in the reliability and
15 accuracy of patient experienced data for regulatory
16 decision making; we want to reduce regulatory
17 uncertainty for the sponsor by consistency applying
18 standards; and we want to promote rapid and consistent
19 adoption of new guidance, processes and resources
20 through good communication, both internal and external
21 to FDA. And finally, we hope to see sustained
22 incorporate of patients' experience in drug

1 development and decision making, make it a standard
2 practice.

3 We have multiple efforts underway to
4 help with this vision becoming reality. In the
5 interest of time, I'm only going to touch on two
6 during this talk.

7 So one way we are working on
8 incorporating patient input as standard practice is by
9 providing guidance on methodologically sound ways to
10 collect and use patient experience data so that it can
11 be used to inform drug development. We have a series
12 of four guidance documents, each of which is
13 accompanied by a workshop to inform its development.
14 We've published the first two guidance documents, held
15 a public workshop to inform the development of the
16 third guidance.

17 And tomorrow in this very room, we'll
18 be holding a public meeting to hear from stakeholders
19 regarding guidance four, which will provide guidance
20 on incorporating clinical outcome assessments into
21 endpoints for regulatory decision making. We would
22 encourage all of you to attend. On-site registration

1 will be available, and the meeting will also be
2 webcast.

3 Another way we are working to encourage
4 the incorporation of patient input into regulatory
5 decision-making is through the establishment of the
6 Standard Core Clinical Outcome Assessments and their
7 Related Endpoints Grant Program. As patient focused
8 drug development efforts began maturing, we noticed
9 that there are currently little -- there's currently
10 little coordination in efforts to develop COAs,
11 including within a given disease area.

12 There's a great deal of duplication of
13 efforts and a diversity of measures; proprietary tools
14 are being developed at great costs, but then they are
15 limited in affordability and sustainability. FDA
16 reviewers may currently receive multiple independent
17 COAs for review, each of which takes time to
18 understand and evaluation. And we're also seeing
19 variable quality of the tools and resulting data that
20 has the potential to limit the tool's utility for
21 regulatory decision making.

22 So FDA's grant program will enable

1 development of standard core sets of measures of
2 disease burden and treatment burden for a given area
3 that will be made publicly available. A standard core
4 set can include different types of COAs and their
5 related endpoints that assess a minimum list of
6 impacts that matter most to patients; are likely to
7 demonstrate change, including differences in trial
8 arms related to disease burden, treatment burden and,
9 if applicable, physical function, and should be
10 reported in a clinical trial.

11 FDA expects grantees to conduct a well-
12 managed, transparent, and methodologically sound
13 process that provides for consistent application of
14 appropriate methods, consideration and use of vetted
15 publicly available measures, milestone workshops
16 engaging key stakeholders, and milestone work products
17 that are made publicly available.

18 So in mid-September, we awarded three
19 of these grants, and you'll hear more about each of
20 them in a moment. We are really excited to be working
21 with our grantee teams. We're very impressed with the
22 strong teams they've put together. They all have a

1 combination of expertise in clinical areas, COA
2 methodologies, and a strong commitment to including
3 the patient community as they develop the core sets.

4 To touch a little bit on the
5 administrative portion of the grants, these grants are
6 funded under a cooperative agreement that has the FDA
7 and the grantee team guided by the grant PI, who is
8 ultimately responsible, working together towards a
9 common goal. Within the FDA, we have multiple
10 internal stakeholders involved. These stakeholders
11 include our clinical review divisions, our COA staff,
12 our biostatisticians, and anyone else who may be
13 interested in the success of this program.

14 These grants are funded using a two-
15 phased approach: the first phase is the UG-3 phase,
16 which is a one- to two-year phase focusing on planning
17 activities; the second phase is the UH-3 phase, which
18 is the implemental phase where the COA sets will be
19 developed and validated. A high-level review will
20 take place between the first and second phase to
21 ensure that the projects are moving in the right
22 direction.

1 We've also designed into the grant
2 multiple opportunities for stakeholder input. And as
3 I mentioned, we'll be holding twice yearly public
4 meetings with an opportunity for stakeholders to ask
5 questions and provide feedback, both as part of the
6 meetings or by submitting feedback to the public
7 docket. Each grantee has put together an external
8 technical advisory committee made up of disease-
9 specific experts, COA experts, biostatisticians,
10 patient experts, and other technical experts as
11 appropriate who oversee and monitor each specific
12 project.

13 And because we realize that many trials
14 are multi-regional or are used by multiple health
15 authorities to make decisions, we have convened a
16 scientific policy board to bring a global perspective
17 to the standard core COA development process. The
18 board is currently made up of representatives from the
19 FDA, NIH, AHRQ, CMS, the VA, and the HLWPMDA in Japan
20 and EMA in Europe, and we anticipate that this will
21 expand.

22 In closing, I would like to thank you

1 all for giving your time to this project. It's
2 something that's very important to the FDA, and we are
3 looking forward to collaborating with excellent teams,
4 and we look forward to your feedback because we
5 understand that we can't do this in a vacuum. Here is
6 a link to the additional information on the COA grant
7 page in case you have some spare time and would like
8 to do some reading. Thank you all for your attention.

9 And at this time, I would like to
10 invite Dr. Kanecia Zimmerman of Duke University to the
11 podium to discuss the clinical outcome assessments for
12 acute pain therapeutics in infants and young children,
13 COA-APTIC grant. Thank you.

14 KANECIA ZIMMERMAN: Good morning. On
15 behalf of the COA-APTIC team and my colleague Dr.
16 Bryce Reeve, we are really excited to be here today
17 and to have the opportunity to present. We're really
18 excited that we were one of the awardees and hope that
19 we get to learn a lot from you guys as we move
20 forward.

21 Over the next several minutes, we hope
22 to tell you a little bit more about why we're

1 motivated to do this project, what are goals really
2 are for this project, give you an overview of our team
3 members, and the aims and milestones throughout the
4 phases. We also hope to tell you a little bit about
5 the stakeholder engagement plan that we have planned.

6 So many of you are already aware, pain
7 among infants and young children is disproportionately
8 underrecognized and undertreated. There are a number
9 of reasons for this: one is that few medications to
10 treat pain in this population are actually FDA labeled
11 or EMA labeled. A lot of it has to do with the fact
12 that we have difficulty doing clinical trials in
13 children period, let alone in this particular
14 population.

15 There are a number of reasons for not
16 having the efficacy and safety information: one is
17 that we can't really just take the information from
18 adults and translate it to children. That's because
19 we know that there is immaturity, and children are
20 rapidly growing and rapidly developing over time.
21 They have rapidly changing systems of metabolism,
22 elimination, and even the receptors. So the drugs may

1 not work the same in adults as they do in children and
2 even older children as they do in infants.

3 There are also many ethical limitations
4 in conducting clinical trials in children. Can you
5 imagine not being able to consent a child, yet not
6 giving them pain medication because you want to test
7 whether or not the drug is efficacious and want to
8 make sure that you have a placebo arm. It really
9 isn't something that we can actually do.

10 The other problem is that these
11 children can't really talk to us; therefore, we don't
12 really know if this is coming from pain or is it
13 coming from a wet diaper or just general irritation.
14 So these are some of the limitations that have kind of
15 plagued this area to date.

16 We believe that really high-quality
17 COAs and standardized well-justified endpoints can
18 help mitigate some of the limitations of the current
19 clinical trials. Although many people have done a lot
20 of work in this area and we definitely will stand on
21 their backs, to date, there are no well-accepted core
22 set of COAs or endpoints for this particular

1 population.

2 So our goal as a COA-APTIC team is to
3 identify or develop core sets of high-quality COAs and
4 endpoints for assessment of acute pain and other
5 relevant outcomes for use in clinical trials of pain
6 therapeutics in infants and young children.

7 We are really fortunate to have, I
8 think, a really strong team with expertise both in the
9 clinical realm, in the measurement realm, and even in
10 dissemination. I lead the clinical team at Duke.
11 Bryce Reeve, my colleague, leads the measurement team.
12 And then we have the Duke Clinical Research Institute
13 communications team, who is involved in dissemination.
14 I'm really pleased to have Emily (indiscernible) and
15 Courtney Mann here today as our team members as well.

16 We have convened an external technical
17 advisory committee really made up of a diverse group
18 of people. We're super-excited about the opportunity
19 to work with people who can think outside of the box,
20 which I think is really needed within the context of
21 this space. We have three parent advocates who are
22 very excited to share their stories about children

1 with sickle cell disease and being a parent of a
2 patient with osteogenesis imperfecta or congenital
3 heart disease.

4 We're pleased to have Robyn as our
5 regulatory expert. Ernest Kopecky, who is the vice
6 president of TEVA will serve in an industry role. Amy
7 Ohmer and Leanne West come from the International
8 Children's Advisory Network and will be very important
9 in thinking about how we do advocacy and how we think
10 about patient advocacy and how we implement this in
11 the future.

12 Dr. Frank Rockhold is an expert in
13 biostatistics. He also has done a lot of returner
14 results work, as well as data sharing and data
15 standards, so will be very helpful in thinking about
16 endpoints in general.

17 Dr. Bonnie Stevens and Dr. Gary Walco
18 are really forces within this particular area. Dr.
19 Bonnie Stevens, in particular, has focused a lot on
20 neonatal pain, and Dr. Gary Walco has been the co-
21 chair of pediatric pain research consortium within
22 Action, within I'll talk about a little bit later.

1 Dr. David Warner is a practicing
2 pediatric anesthesiologist who really will help us
3 really understand some of the nuances in that
4 particular space. And I mentioned Leanne West with
5 iCAN.

6 So together, we intend to really put
7 together the scientific pieces to make sure that
8 people are excited and able to invest in pediatric
9 trials of acute pain therapeutics, particularly for
10 this population.

11 We are fortunate to be able to leverage
12 a number of resources that are led by Duke teams. The
13 Pediatric Trials Network is a network that is
14 sponsored by the NICHD. Under BBICA legislation, NICHD
15 was really charged to create an infrastructure for
16 investigators to conduct clinical trials that improve
17 pediatric labeling and child health.

18 I am chair of the steering committee
19 for the Pediatric Trials Network and oversee the day-
20 to-day activities of this network. And I'm really
21 pleased to say that we have conducted more than a
22 hundred clinical studies -- or we have more than a

1 hundred clinical sites, have more than 40 clinical
2 studies, and multiple collaborators really across the
3 globe. We've studied in more than 18 therapeutic
4 areas, enrolled more than 8,000 children, submitted 26
5 packets to the FDA for labeling update and have
6 resulted in 11 label changes. So we really think this
7 is a strong foundation for being able to connect with
8 sites and being able to connect with patients.

9 We have sites in 43 states. The
10 coordinating center is at Duke, as I mentioned before.
11 The Duke Center for Health Measurement also is a gem,
12 we think, at Duke. The Center for Health Measurement
13 is led by Bryce, and it partners with clinical
14 researchers and healthcare providers to bring patient
15 and caregiver voices really into care planning,
16 treatment decisions, and health policy.

17 We have many methodological
18 specialties, including psychometrics, statistics,
19 qualitative research, health preferences, stakeholder
20 engagement, and we evaluate people from pediatrics to
21 geriatrics across therapeutic areas.

22 The goal of the Center for Health

1 Measurement, regardless of COA-APTIC, is really to
2 engage multiple stakeholders to determine endpoint
3 models and outcome measures, and to select or design
4 COAs to use in research studies or healthcare
5 settings. They are very interested in using stated
6 preference methods to capture patients and caregivers'
7 concerns, values, and preferences. So together, I
8 think we really have a very strong core.

9 We are also fortunate. There have been
10 people in this space already that we can work with and
11 we can kind of learn from the thoughts that they've
12 already put together. The analgesic, anesthetic, and
13 addiction clinical trial translations, innovations,
14 opportunities and networks for action has formed a
15 consensus meeting or previously formed a consensus
16 meeting to think about clinical trial designs and
17 models for analgesic medications in neonates, infants
18 and toddler, actually up to age 18. But really
19 provided some guidance in this group that we think
20 will be very helpful.

21 Pediatric impact group is a pediatric
22 initiative on methods, measurement and pain assessment

1 in clinical trials that has really thought a lot about
2 core outcome domains to consider when designing
3 clinical trials in this age group. They have focused
4 a lot on children who are older, but have also
5 provided some guidance for the younger group as well.

6 So with that foundation, we have a
7 plan, a very fairly ambitious detailed plan here.
8 I'll go through all of these in the next couple of
9 slides.

10 So in year one, we really want to
11 identify outcomes important to stakeholders in the
12 context of pediatric acute pain. We also are very
13 interested in making sure ETAC kind of trains each
14 other, that everyone is up to speed on what things
15 mean and that we're speaking the same language. We
16 have a number of ways that will do this. We will do a
17 literature review for the outcomes. We will do
18 concept elicitation to really identify the outcomes
19 that are important to people, and then the external
20 technical advisory we'll talk a little bit more about.

21 So the literature review really
22 primarily for this phase will focus on outcomes and

1 endpoints that are used to evaluate (indiscernible)
2 for acute pain and/or distress in infants and young
3 children and really focus on the zero to less than 3-
4 year-old age range.

5 We believe that as a byproduct of some
6 of the things that we'll pulling, we will also gather
7 information on COAs that have been used in the past to
8 assess the identified outcomes and endpoints. We will
9 get some idea of what people think by way of did you
10 identify the outcome as a primary, secondary, or
11 exploratory outcome; what is important to you based on
12 those things. Are there -- is there heterogeneity in
13 the outcomes and the endpoints that have been used
14 kind of across ages, across populations, et cetera.
15 And then how have people in the past differentiated
16 pain expression and behaviors from other distress
17 expression and behaviors, so cry or movement and
18 things of that nature.

19 The concept elicitation interviews, we
20 intend to do one-on-one interviews with at least 24
21 clinicians and 36 caregivers. We will recruiting from
22 PTN sites, such that we will really have an emphasis

1 on geographic, socioeconomic and demographic
2 diversity. We want to make sure that we're
3 representing everyone and everyone's voices. We're
4 hoping to have equal representation of infants and
5 young children, ranging from the zero to 36-month age
6 range and will likely also concentrate on the zero to
7 two-month age as well within this particular group.

8 Some questions that we intend to ask,
9 for example, would be: how does a child who is zero to
10 less than 3 years of age express pain, or how does
11 your child in this age range express pain; how do you
12 actually determine the severity or intensity, via
13 their behaviors or their movements, their
14 vocalizations or cry, or maybe even their facial
15 expression; how can you actually tell the difference
16 between pain and other types of distress. That goes
17 to you mom, or that goes to you, you know, clinician.
18 And then how do you know when an intervention for pain
19 is successful; what is your goal for success?

20 As I mentioned, we're also very
21 interested in this phase of making sure everyone's on
22 the same page. As I mentioned as well, our ETAC is

1 very diverse and a number of people have not even
2 stepped in this space at all, so it's going to be
3 very, very important that we, you know, speak the same
4 language. We will have our ETAC train on
5 perioperative pain management and assessment, talk
6 about the long-term effects of acute pain experience
7 and quality of life so people really understand why in
8 the world we might be doing this. Thinking about how
9 you develop outcomes and endpoints in clinical trials.

10 There will be opportunities to engage
11 patients, stakeholders, and research and practice, and
12 we really want to learn about what those -- what has
13 worked before, even outside of this space. What is
14 the parental perception of the child pain experience?
15 And what is the role of industry or what does industry
16 even think about this space at all; are they
17 interested, how do they think they should move forward
18 or we should move forward. What is the current state
19 of pain assessment based on people and experts who
20 already have kind of been there, and what are the
21 challenges and next steps that we haven't thought of
22 before?

1 So in AIM two -- or year two, we hope
2 to then identify the characteristics of COAs for each
3 outcome once we have identified our list of outcomes.
4 We then will concentrate on evaluating the quality for
5 each of these COAs. And as we go through the process,
6 we intend to identify where the gaps are; we will
7 design the UH-3 phase based on the gaps.

8 In the UH-3 phase, we really hope that
9 we will do some implementation, that we'll do
10 qualitative and quantitative evaluation in order to
11 really provide some additional evidence for the COAs
12 that we've picked for the outcomes that we've
13 identified that are important to people. We will
14 intend to provide the documentation to support this
15 and make it publicly available.

16 Throughout this process, we have a plan
17 for engaging our stakeholders, both through our ETAC,
18 through our respective teams with the PTN, as well as
19 the Center for Health Measurement. We're going to use
20 the websites that are already there because a lot of
21 people already come to them and visit them and are
22 very interested in what we're doing. We intend to

1 disseminate this information through scientific and
2 public meetings, through publications of course, and
3 then collaboration with stakeholders. We're fortunate
4 that we are already in talks with Action and the
5 Impact Group to see how we might be able to interweave
6 our efforts.

7 Thank you again for the opportunity to
8 present today. I'm happy to take any questions, and
9 you are more than welcome to contact any of us moving
10 forward. Is there anything from the Webix?

11 MEENA SAVANI: None at this time.

12 KANECIA ZIMMERMAN: Okay, thank you.

13 ROBYN BENT: Thank you so much, Dr.
14 Zimmerman. I would now like to invite Dr. Richard
15 Lipton of Albert Einstein College of Medicine to the
16 podium to talk about the Migraine Clinical Outcome
17 Assessment System Grant Program, or MiCOAs.

18 RICHARD LIPTON: Well, thank you. So
19 the program that I'm going to present is a little bit
20 different than the other two programs you're going to
21 be hearing, in the sense that we're focusing on a
22 disease, rather on a symptom. And because of that,

1 I'm going to spend just a few minutes talking about
2 migraine, which I know, although I spend much of my
3 life thinking about migraine, that is not true for
4 most of the people in the room.

5 So migraine is certainly an
6 extraordinarily disorder by any standard. Twelve
7 percent of the global population has migraine.
8 Estimates from the World Health Organization Global
9 Burden of Disease Program estimates that there are a
10 billion people in the world who have this condition.

11 And, of course, like many conditions,
12 migraine is characterized by a relatively broad
13 spectrum of severity. At one end of the spectrum,
14 there are people who have attacks less than once a
15 month that respond well to over-the-counter
16 medications and don't produce disability; and at the
17 other end of the spectrum, there are people who have
18 migraine attacks almost every day who are completely
19 disabled by headache, unable to work, unable to engage
20 in family life and so forth.

21 So migraine is a disorder characterized
22 by brain sensitivity. It's a genetic disorder. It's

1 a disorder that's characterized by a group of symptoms
2 that travel together in various combinations in people
3 who have the disorder. Pain is the most obvious and
4 the most disabling symptom of migraine, and the pain
5 is usually one sides, pulsatile, exacerbated by
6 physical activity.

7 The pain is inevitably accompanied by
8 other features, and the migraine-defining features
9 that are part of the international classification of
10 headache disorders include nausea or vomiting,
11 photophobia, sensitivity to light, and phonophobia,
12 sensitivity to sound, as well as auras where auras are
13 neurologic symptoms that typically evolve slowly and
14 last between 15 minutes and an hour. And any given
15 person with migraine may have various sets of these
16 symptoms.

17 Of course, one important hallmark of
18 migraine is that it's a chronic disorder with episodic
19 attacks. And by that, I mean the most prominent and
20 disabling feature of migraine occurs during attacks.
21 But between attacks, people have an enduring
22 predisposition to attacks and actually have

1 disability, functional limitations, anxiety,
2 difficulty with planning between attacks as well.

3 According to the Global Burden of
4 Disease, migraine is the world's second leading cause
5 of disability, as measured by the metric disability
6 adjusted life years. It disrupts health-related
7 quality of life. Part of the reason that migraine is
8 so disabling is that it's a condition that typically
9 begins in adolescence or early adult life, and people
10 with more severe forms of migraine may have the
11 disorder throughout their life span during their peak
12 productive years.

13 One estimate of the cost of migraine in
14 the United States is at a cost about \$20 billion per
15 year. This is an older estimate that includes both
16 direct and indirect costs, and estimates are often
17 much higher. Unlike most disease advocates, I
18 selected a low end estimate rather than the highest
19 estimate I could find, so I would consider this a
20 lower bound estimate.

21 So like other chronic disorders with
22 episodic attacks, treatment of migraine is generally

1 divided into two categories: acute treatments, which
2 are given at the time of the attack to relieve pain
3 and restore function; and preventive treatments, which
4 are given independent of the timing of attacks to
5 reduce the frequency and severity of attacks and
6 perhaps to reduce medication overuse.

7 So since 1990, development of
8 treatments for migraine has been tremendously
9 successful. So I was thinking about the number of
10 drugs that have been approved for migraine since 1990,
11 and it's seven triptans, two NSIDS, three devices, and
12 one new drug in a class called ditans; and on the
13 preventive side, there have been two anti-epilepsy
14 drugs, three monoclonal antibodies, and several
15 devices that have been approved.

16 So there's been a tremendous expansion
17 of therapies for migraine on the one hand, but on the
18 other hand, we're continuing to use the same endpoints
19 that have been used throughout my rather long career
20 in this field.

21 So when it comes to measuring acute
22 treatment effects, the typical regulatory endpoints

1 focus on pain and on the symptoms associated with
2 pain. So although the trip- -- and generally the way
3 these trials are done is patients are asked to wait
4 until pain is moderate or severe. And they then take
5 a treatment, have an electronic diary and record pain
6 and associated symptoms at relatively frequent
7 intervals over the first couple of hours, and then
8 much less frequent intervals after that.

9 And in these studies, patients are
10 typically allowed to rescue two hours after taking
11 their therapy. The typical primary -- one typical
12 primary endpoint is pain freedom two hours after a
13 drug is delivered, and that is certainly a regulatory
14 endpoint that served the field well on the one hand.
15 But on the other hand, I've never seen a patient who
16 says, well, what I really care about is what my level
17 of pain is at two hours and I don't care what happens
18 before that and after that, so we may be leaving
19 information on the table.

20 We also measure most bothersome
21 symptom, which is a patient selected endpoint,
22 selected from among nausea, sensitivity to sound and

1 sensitivity to light. And the second co-primary
2 endpoint in most recent migraine trials has been
3 freedom from the most bothersome symptom at two hours.
4 We also look at sustained pain freedom; does the pain
5 go away and stay away? And there are some PROs that
6 are used for acute treatment trials, either to assess
7 the benefits of individual attacks or to assess the
8 longer-term benefit of treating multiple attacks over
9 time.

10 The challenges are that many of these
11 endpoints were really developed without a patient
12 voice. Most regulatory trials focus on a single
13 attack where people treat multiple attacks in the real
14 world. When we prescribe an acute medication,
15 patients use it over and over again. And regulatory
16 endpoint -- primary regulatory endpoints certainly
17 don't measure consistency of treatment effect, focuses
18 on a single point of time when time, of course,
19 matters, and relatively little attention is given to
20 disability and quality of life.

21 On the prevention side, the usual
22 primary endpoint has changed from baseline in monthly

1 migraine days or monthly headache days. This is
2 dichotomized into a 50 percent responder rate, which
3 is the proportion of people whose headache frequency
4 is reduced by 50 percent or more over one month or
5 three months.

6 We heard in meetings yesterday with
7 Eric Bastings and Nicholas Kozar that they see a major
8 unmet need in the migraine space or measures that will
9 allow us to better assess disability or functional
10 status in the context of regulatory prevention trials,
11 and the team certainly agrees that that is one very
12 important area of unmet need.

13 The challenges in prevention are
14 endpoints that, again, the endpoints were largely
15 developed without a patient voice, that defining
16 migraine and headache days is difficult, that much of
17 the benefit of prevention goes unmeasured in the
18 regulatory endpoints, and that for the most part
19 disability and quality of life are not attended to.

20 So our objective, and this slide
21 projects rather dark, but our objective is to develop
22 clinical trial endpoints for patients -- with patients

1 and for patients. So the aims then of the MiCOAs
2 project in phase one are: to build a team of advisors,
3 which we've done; to develop an initial list of
4 endpoints that have been used, and we've completed
5 that task; to conduct a systematic literature review
6 of all the clinical trials that have been conducted on
7 migraine on the acute and prevention side, and based
8 on that literature reviewed, refine our list of
9 endpoints that have been used in the past.

10 And then to talk to people with
11 migraine and make recommendations for what are the
12 things -- what things are the most important things to
13 measure. From there, we will talk to people with
14 migraine about how we can best capture the recommended
15 endpoints in a way that makes sense to patients. We
16 plan to conduct two rounds of data collection, one for
17 acute treatment and one for preventive treatment, to
18 study the psychometric quality of the measures that we
19 develop and to establish those measures. And then
20 finally, our goal is to make the measures we develop
21 available to people who want to use them.

22 One of our partners in this process is

1 an organization called CHAMP, the Coalition for
2 Headache and Migraine Patients. This is an
3 organization that brought together something like 40
4 separate patient organizations. And their goals are
5 to support people with headache, migraine and cluster,
6 to bring together stakeholders to more effectively
7 help people, and to identify unmet needs for those
8 with headache disorders, and to work to better support
9 patients and caregivers.

10 So this group reaches more than a
11 million people with migraine. And one of the members
12 of our ETAC is Katie Golden and she is a
13 representative of CHAMP, and you will be hearing more
14 from her a little bit later this morning.

15 So as we try to develop clinical trial
16 endpoints with patients, for patients, patients and
17 people with migraine are being incorporated into this
18 process at various stages. So in AIM three, we're
19 going to do qualitative studies focused on better
20 understanding what endpoints make sense to patients.

21 In AIM four, we'll do more qualitative
22 work focusing on the development of a new endpoint or

1 new endpoints. And there are many endpoints out
2 there, so we're certainly not interested in making
3 change just for the sake of making change. And we
4 will carefully evaluate the tools that have been
5 developed, and to the extent that they're fit for
6 purpose, we'll be conservative. To the extent that
7 what we hear from patients mandates change, then we'll
8 make those changes.

9 A couple of areas of migraine burden
10 that have not been well measured that were highlighted
11 in our discussions with FDA yesterday were the
12 cognitive burden of migraine. So it turns out that
13 throughout the migraine attack, many people have
14 cognitive problems. And the other thing that was
15 emphasized by FDA yesterday, which I hear from
16 patients very often, is about what's called the
17 interictal burden of migraine, the burden between
18 attacks.

19 And so, those are two areas where we
20 particularly feel that additional development may be
21 needed, and we will test that hypothesis in the
22 qualitative work that we do.

1 And then in AIM five, we'll do two
2 quantitative studies to refine measures as needed to
3 ensure that we have reliable fit-for-purpose measures.
4 And as I mentioned already, Katie Golden, who is a
5 patient advocate, is part of our ETAC.

6 So our goal then is to develop
7 endpoints and their measures that accurately reflect
8 patients' experience using patient input and
9 collaboration and the best available psychometric
10 methods. And with that, I'd like to stop, thank you
11 for your attention, and see if there are any
12 questions.

13 MEENA SAVANI: We do have a question
14 from the web. The question is: why do you think that
15 existing migraine COAs are not fit for purpose?

16 RICHARD LIPTON: Well, you know, so I
17 don't want to prejudge what we hear from focus groups.
18 There are a number of measures that are out there.
19 I've, you know, worked on many of them over the past
20 30 years and, you know, I'm not here to criticize
21 existing measures.

22 The issue is ensuring that the measures

1 that we recommend really reflect the patient voice.
2 So some of the measures have a three-month recall
3 interval, and that may be an interval that's too long
4 to be credible; some of them have a one-month recall
5 interval, and that may be stretching the period over
6 which a patient with migraine can report their
7 experience; some of them are daily measures. One
8 major issue is distinguishing ictal and interictal
9 burden. Another major issue is making sure we capture
10 all of the domains that are important to patients,
11 including cognition.

12 So, you know, I'm not here to criticize
13 the PROs that have been developed. Our purpose is to
14 validate those PROs, listening carefully to the
15 patient voice, and we hope confirm the utility of
16 what's out there or build on the utility of what's out
17 there by refining it.

18 PAUL: Hello, Paul (indiscernible),
19 Meditation Solutions. I'm curious to your thoughts
20 around specifically for acute measurement, the actual
21 burden on the patients of just reporting it at that
22 time. We recently just finished some usability

1 testing of an electronic solution for capturing data
2 from patients. And some of them reported concerns
3 around actually interacting with an electronic device
4 while in the midst of a migraine, and I suspect that
5 could extend to paper and pencil as well potentially
6 being challenging. Just curious to your thoughts on
7 that.

8 RICHARD LIPTON: Yeah. So, you know,
9 so one of the hallmarks of migraine is sensitivity to
10 light and sound, so in most migraine trials, data is
11 captured using electronic diaries. And so, the task
12 we give patients, both in acute and preventive
13 studies, is listen to the alarm go off on your diary,
14 then tell us how much your head hurts while you look
15 at a brightly lit screen. So, yeah, so there are
16 challenges. I mean, obviously, the advantage of real-
17 time data capture is that it circumvents the recall
18 issues that have people recall their experience.

19 You know, one approach is to use a
20 daily measure where people record their experience
21 over the course of the day. The most common approach
22 is to use daily diaries with multiple assessments per

1 day. And we will talk to patients about how they feel
2 about interacting with their smart phones or with
3 their computer screens to try to get a handle on that.
4 I think it's an important issue. Other questions?

5 Well, if not, on behalf of the MiCOAs
6 team, I want to say --

7 MEENA SAVANI: We have one more
8 question, sorry, and then you can wrap up.

9 RICHARD LIPTON: Okay.

10 MEENA SAVANI: The last question is:
11 most trials submitted to the U.S. include
12 international sites. Sometimes COAs developed in the
13 U.S. do not work the same way outside the U.S. How
14 are the projects, including information from patients
15 outside the U.S.?

16 RICHARD LIPTON: Yeah. So the scope of
17 our focus groups and qualitative research will be
18 limited to the U.S. We're well aware that drug
19 development often occurs on an international basis,
20 and we're interested in developing measures that will
21 meet regulatory standards of FDA, but also regulatory
22 standards of other agencies.

1 There is a meeting later today that
2 includes representatives of regulatory agencies
3 outside the U.S. We're going to do an evaluation of
4 the measures we develop for translatability, but
5 actually doing translation and validation in languages
6 other than English is outside the scope of what we're
7 going to do.

8 WOMAN: (indiscernible) from Genentech.
9 A quick question. You mentioned function, and in the
10 spirit of co-concept because functions of interest for
11 industry. Do you plan on interacting with the other
12 group working on function so that we won't have a
13 migraine instrument between function, but who would
14 have a co-concept between function across different
15 (indiscernible) area? What is the plan for your
16 function part of measurement?

17 RICHARD LIPTON: Well, so, just as in
18 measurement of quality of life, there are generic and
19 disease specific measures. In measuring functional
20 status, one can envision generic and disease specific
21 measures. The group developing measures of disability
22 are very much taking an approach that's focused on

1 developing a generic measure that will work across a
2 range of diseases.

3 Our focus is very much on developing a
4 disease specific measure. You know, obviously an
5 advantage of disease specific measures is that we
6 might be able to be more sensitive to particular
7 problems that are very burdensome in migraine. The
8 advantage of having a disease -- a generic measure is
9 that you can compare functional status in disability
10 across diseases on a common yardstick. To the extent
11 that the measure works equally well across a range of
12 diseases, we will certainly interact with the
13 disability group.

14 My co-PI on this project, R.J. Wirth,
15 has worked with the disability group extensively.
16 I've not had that privilege, but we will certainly
17 endeavor to learn from them and keep those two
18 perspectives in mind. But our goals are really quite
19 different because we're focusing on a disease and
20 they're focusing on functional status, each of which
21 has advantages and disadvantages, I would say.

22 WOMAN: Thank you.

1 MEENA SAVANI: And we do have another
2 question. Many times, research includes patients as
3 the people we get information from, and others work
4 toward more partnership. How do you envision patients
5 will be engaged in your study design and information
6 dissemination?

7 RICHARD LIPTON: Right. Well, so, you
8 know, we do have a patient advocate on our advisory
9 board. We do plan on running multiple focus groups
10 and some surveys that involve patients to ensure the
11 patient voice is represented at multiple stages in the
12 process. And we hope that our patient advocacy
13 partners will, with their broad reach, will play a
14 major role in disseminating our findings.

15 We're planning on developing a website
16 of our own to make the measures that emerge from this
17 process accessible. We're hoping to publish the
18 systematic reviews that we do on the way to developing
19 a final measure, and we're open to other ideas if the
20 questioner has any.

21 MEENA SAVANI: And another question
22 that we also welcome anyone from the audience to

1 comment on as it's more general. What areas do you
2 think would benefit from development of COA core
3 outcome sets? So more of a general question.

4 RICHARD LIPTON: Yeah. Well, so from
5 my highly biased perspective, no area is more
6 important than migraine. But, you know, yeah, I don't
7 know. I will open that. I mean, obviously, there's a
8 need in many areas. I think, you know, Alzheimer's
9 would be a great area for additional development.

10 And I think the sort of, you know, the
11 fascinating thing to me about this pilot project, and
12 I think the wisdom of the people who set this up, is
13 that built into this are two competing strategies: one
14 is focusing on a domain of measurement, like pain or
15 functional status, and the other is focusing on a
16 disease. And, you know, ultimately, those approaches
17 need to converge as we measure domains in people with
18 particular diseases. And I don't know if anyone else
19 has something to add to that.

20 R.J. WIRTH: If I could, it's outside
21 the scope of the migraine. It's R.J. Wirth, I'm with
22 the migraine project. But I think finding an area

1 that could incorporate wearables of some kind would be
2 really interesting, just to figure out -- I mean, that
3 sort of landscape right now is so diverse and there's
4 no really clear structure about how do you build an
5 endpoint around a wearable device that's sort of well-
6 accepted and well-established. So something like
7 Parkinson's or some other area that would allow us to
8 sort of explore that more, I think would be great.

9 RICHARD LIPTON: Any other questions?
10 Well, if not, thank you so much for your attention and
11 for this opportunity.

12 ROBYN BENT: Okay, so thank you very
13 much, Dr. Lipton. And my apologies to the people
14 online, but I think that we're going to, instead of
15 taking a break that was scheduled after Dr. Lipton's
16 talk, I think we're going to move straight into the
17 NUCOAT teams talk, so that we'll just add a little bit
18 of extra time to our panel discussion if that's
19 something that evolves organically.

20 So right now, I would like to invite
21 Dr. Sara Shaunfield from Northwestern University to
22 the podium to discuss the Northwestern University

1 Clinical Outcome Team Assessment Grant Program, or
2 NUCOAT.

3 SARA SHAUNFIELD: Hi, thank you. Sara
4 Shaunfield here. I'm here to present on behalf of my
5 team members for the Northwestern University Clinical
6 Outcome Assessment Team Grant Program, which we
7 bovinely refer to NUCOAT. I'm presenting on behalf of
8 our principal investigator, David Cella, who is
9 actually in Japan today, so I am very excited to be
10 here and share this with you.

11 The main objective of NUCOAT is to
12 refine and test a set of cross-cutting measures for
13 physical function that can capture a range of physical
14 function impact from mild to severe, and that are
15 appropriate for use in chronic conditions and rare
16 disorders.

17 You may be asking yourself why physical
18 function is important. Disease-related symptoms and
19 treatment side effects have a great impact on one's
20 ability to function and lead a normal life. With
21 physical symptoms, normal is often defined by one's
22 ability to move about freely and to engage in

1 activities of daily living. So we feel that this
2 provides a good opportunity for a cross-cutting
3 measure of physical function across diseases and will
4 have impact for a lot of patients.

5 So I'm going to start by introducing
6 our team, and then I'll give an overview of our UG-3
7 aims, the organizational structure and committee
8 membership, as well as some of the measurement systems
9 that will form the foundation of the work that we'll
10 be doing, and then we'll dive into some of the details
11 of the project.

12 So here we have our team. At the top,
13 we have the members of the Northwestern University.
14 David Cella there is the principal investigator. And
15 across the Northwestern University team, we have a
16 range of expertise in the development and validation
17 and application of patient reported outcome measures
18 and performance outcomes measures, and specifically,
19 the measurement systems that form the basis of this
20 work.

21 In addition to the Northwestern team,
22 we also have representatives from the National

1 Organization for Rare Disorders, NORD; representing
2 them, we have Vanessa Boulanger and Allison Seebald,
3 who are very informative and helpful throughout this
4 decision making and planning process. We also have
5 representation from Aging in Motion with Jack
6 Guralnik, and the Alliance for Aging Research from
7 Ryan Carney. And these bring perspectives of physical
8 function, epidemiology and policy.

9 And this is, we'll dig into this a
10 little bit later, but these are just a preview of some
11 of the different stakeholders that we have involved in
12 this. And you'll see that we have valuable
13 perspectives from consultants and stakeholders,
14 ranging from payors, regulators, pharmaceutical,
15 patient and caregiver representatives, and then
16 patient reported and performance outcome measure
17 expertise.

18 So as we've discussed today, the
19 project is divided into two phases, the UG-3 and the
20 UH-3. For the UG-3 AIMS, I'm going to talk about the
21 three AIMS that we've proposed.

22 So for the first AIM, we're going to

1 convene stakeholders, including patients, care
2 partners, clinicians, measurement experts, payors,
3 regulators and industry representatives around the
4 topic of physical function. And when we're talking
5 about physical function, we're talking -- we are
6 defining it as one's ability to carry out activities
7 that require physical capability. And this can
8 involve anything from daily self-care activities to
9 more vigorous activities that would require movement,
10 strength and endurance.

11 For our second AIM, we are proposing
12 six model conditions based upon this planning and
13 exploratory work here in this UG-3 phase. So at the
14 end of this, we'll have -- we will be able to propose
15 six model conditions. We want to propose three
16 sarcopenia and three rare disorders in which we can
17 test and measure cross-cutting clinical outcome
18 assessments of physical function that cover a range of
19 type and severity of limitation, and we'll also
20 identify gaps in an of our proposed measures.

21 I think it's important to here to note
22 that for sarcopenia is defined as an accelerated

1 wasting of muscle; it's just kind of a general
2 definition. And sarcopenia can be associated with a
3 number of things and can occur on its own with aging
4 or is often associated with certain chronic
5 conditions.

6 Our third AIM is to propose interim
7 plans and final plans for refining and testing the
8 physical function performance outcomes, based on the
9 promised physical function item bank and physical
10 function performance outcomes based on NIH Toolbox and
11 the short performance physical battery, which I will
12 provide an overview here shortly.

13 So digging in a little bit into our
14 milestones to complete these AIMs. So the first AIM
15 was to convene the stakeholders. And so, here, we're
16 going to motivate, facilitate and retain active
17 participation and involvement, but first we had to
18 establish our committees. As the other groups have
19 done, we've established and nominated participants for
20 our external technical advisory committee or ETAC. We
21 also have assembled a stakeholder engagement group and
22 a clinical expert panel, and I'll provide an overview

1 of these members here briefly.

2 Additionally, we'll establish a project
3 website and semination venues through publication and
4 provide preliminary summaries of physical function
5 assessment options.

6 The second AIM, we will propose the six
7 model conditions to evaluate physical function. In
8 order to get there, we proposed to conduct literature
9 reviews of the impact of physical function across
10 these different conditions, and also looking at the
11 existing patient reported outcomes and performance
12 measures that have been used to evaluate physical
13 function in these conditions. Looking at both patient
14 reported -- I said that. I'm sorry.

15 In addition to the literature review,
16 we will conduct what are some targeted scoping
17 interviews where we'll explore the range of physical
18 function impact and severity across the different
19 conditions, and then also identify similarities and
20 differences to help inform our decision of which of
21 the conditions we'll select for the UH-3 phase so that
22 we can be sure that we have cross-cutting measures

1 that can apply to all conditions.

2 And then finally -- or next, we'll
3 present a gap analysis to the stakeholder engagement
4 group and the clinical expert panel. We'll propose an
5 implementation plan and a final list of conditions.
6 And then finally, we'll develop a sustainability plan
7 for our clinical outcome assessment dissemination and
8 maintenance.

9 For the third AIM of UG-3, we will
10 prepare and present our plan for refining and testing
11 our clinical outcome assessment measures. We'll use
12 feedback from all of our stakeholder groups to guide a
13 well-defined physical function concept definition and
14 the validation process and plans for UH-3. As part of
15 this AIM, we'll develop the protocol for refinement
16 and validation, and we'll develop and submit the
17 revised materials so that, hopefully, we will be able
18 to continue this work in the latter years.

19 So now I'm going to talk to you and
20 show you our organizational chart. In this, you'll
21 see that we have Northwestern University. And above
22 that, we have our scientific policy board and program

1 steering committee. And then to the left, we have the
2 external technical advisory committee, which consists
3 of FTAF program officers and five experts that I'll
4 show you shortly that we nominated. And these three
5 committees are going to have substantial oversight and
6 input throughout the phases, providing redirection as
7 possible and helping us to navigate some of the
8 challenges of developing cross-cutting clinical
9 outcome assessments of physical function in these
10 range of conditions.

11 And then below Northwestern University,
12 you'll see we have our stakeholder engagement group
13 and our clinical expert panel. These also have
14 substantial input in the processes and procedures and
15 will review materials and provide their input before
16 we implement any sort of study -- implement the
17 studies.

18 And then below that, we have our
19 quantitative teams and our qualitative methods teams,
20 and these are the teams that will be conducting the
21 proposed work.

22 So here, we have our committee

1 membership. For our clinical and expert panel, you'll
2 see that we have seven clinicians and experts in
3 rehabilitation and clinical psychology, physical-
4 occupational therapy, and kinesiology. Our
5 stakeholder engagement group is comprised of experts
6 in rare disorders, pharmaceutical industry, patients,
7 caregivers, and payors. And our external technical
8 advisory committee, those that we have nominated to
9 this position, are five experts in patient-reported
10 outcome science, cross-cutting -- cross-cultural
11 validation, statistics, and regulatory strategy.

12 So next, I'll provide background on the
13 measurement systems on which our work is based. So
14 health measures was funded by the NIH, and today is a
15 repository and distribution center for patient-
16 reported outcome measures and performance outcome
17 measures. We have, within health measures, it houses
18 four measurement systems and they assess physical,
19 mental, social health symptoms, wellbeing, physical
20 function, social function, sensory and cognitive
21 function in individuals aged 3 to 85.

22 One of the benefits of health measures

1 is its flexible administration using short forms and
2 computer adaptive tests, which means essentially that
3 the computer will tailor the questions that you
4 receive based upon your responses, and then
5 performance tests of function.

6 The health measures also provides a
7 common metric across the different measurement systems
8 and health conditions and is comparable to the U.S.
9 population. These measurement systems are appropriate
10 for use in clinical research, regulatory practice, and
11 educational settings.

12 These are just an overview of the four
13 measurement system, but for time sake, I'm going to
14 focus on the two highlighted, but the others, we have
15 Neuro-QoL and ASKME. But the highlighted ones, we
16 have PROMIS, which stands for patient-reported
17 outcomes measurement information system, which is a
18 self- and parent-report set of measures for global,
19 physical, mental and social health for adults and
20 children in the general population and for those
21 living with a chronic condition.

22 For this particular project, we're

1 focusing on the physical function item bank, which is
2 a bank of 165 items that's appropriate for a range of
3 conditions and assesses mobility, upper extremity and
4 central body function.

5 Next, the NIH Toolbox, on the other
6 hand -- so PROMIS is a self-report, so it would be,
7 like, pen and paper or computer administrated. And
8 then the NIH Toolbox is a performance test; you're
9 actually performing those activities. And so, NIH
10 Toolbox is a performance test of cognitive, motor and
11 sensory function and emotion in adults and children,
12 again, in the general population and for those living
13 with a chronic condition.

14 And for this particular proposal, we'd
15 be focusing on the motor battery, which assesses
16 dexterity, grip strength, balance, gait speed and
17 endurance.

18 Finally, we have the short performance
19 physical battery, which is a brief set of performance
20 tasks that includes assessments of usual gait speed,
21 balance tests, and tests of lower extremity, which
22 involves raising and standing from a chair. They're

1 very brief, takes about 10 minutes, and is really good
2 for assessing low end of physical function.

3 The SPVB has been linked to patients'
4 perceptions of function and disability. It was
5 developed at the National Institutes of Aging, and one
6 of our co-investigators on the grant was involved in
7 the validation efforts of the project. And it's also
8 free from royalty and permission fees.

9 Okay, so now that we've provided the
10 background, here we have just a visual depiction of
11 the project overview. Above the dotted line is the
12 plans for UG-3, and then below, we have UH-3, and then
13 I'll use this to kind of guide us through the rest of
14 the discussion.

15 So as we talked about, in order to
16 identify the conditions, we are going to conduct
17 literature reviews and scoping interviews. So for the
18 scoping interviews, the plan is to explore a range of
19 physical function limitations, severity, and health
20 related quality of life impact for the candidate
21 conditions.

22 So in collaboration with our expert

1 panel members and the FDA, we've selected six
2 (indiscernible) conditions that are comorbid with
3 sarcopenia, including heart failure, COPD, advanced
4 cancer, hip fracture, Parkinson's disease, and
5 osteoarthritis. We're still working out the fifth
6 rare condition, rare disorder. But currently, we've
7 decided upon achondroplasia, osteogenesis imperfecta,
8 Guillain Barre, fibro dysplasia, and the next one is
9 unknown at this point.

10 Findings of these scoping interviews
11 will complement our gap analysis and literature review
12 and help us to inform the selection of six of out of
13 this 11 set of conditions for a cross-cutting physical
14 function COA.

15 So just a brief overview of some of our
16 procedures. As I said, these are targeted scoping
17 interviews. We are going to conduct approximately
18 three interviews with adult patients within each of
19 these conditions, so we expect to conduct around 33
20 interviews. And within the interview, we will elicit
21 the symptoms and treatment side effects that drive
22 physical function limitations, and we're going to be

1 sure to capture the full range of physical function
2 limitations through probes to make sure that we're not
3 missing any instrumental activities of daily living,
4 mobility, dexterity, axial function, and we're also
5 going to probe about use of assistive technologies and
6 devices.

7 Our data analysis plan is we will
8 conduct a frenetic analysis of the physical function
9 limitations for each condition separately; within
10 this, we're also looking at the subdomains, axial
11 mobility, dexterity. And once we have our list of
12 physical function limitations, we will correlate that
13 with the severity and health-related quality of life
14 importance ratings, and compare those across
15 conditions so that it will help us to select our
16 ultimate six conditions for UH-3.

17 For our literature review, the plan is
18 to identify and describe the impacts of the candidate
19 conditions, both rare disorders and sarcopenic
20 conditions, on the spectrum of physical function.
21 And, again, we'll be looking at anticipated severity,
22 as much as we are able to tell from the literature

1 review to inform these decisions. We're also going to
2 conduct a measure scan to identify existing patient-
3 reported outcomes and performance outcomes, but assess
4 these outcomes within these different contexts so that
5 we can include this evidence and support our decision
6 for a core set of COAs.

7 As we've all discussed, there's a lot
8 of stakeholder engagement, and I wanted to briefly
9 discuss with you our plans for engaging stakeholders
10 and for motivating them. So as we said, AIM one is to
11 convene stakeholders, care partners, patients,
12 clinicians, experts, payors, regulators. And the goal
13 of this is to motivate, facilitate and retain active
14 participation with all of these stakeholder groups
15 throughout this process.

16 In order to do this, we are going to
17 follow the principles set forth by PCORI for
18 stakeholder engagement, in which we will emphasize
19 reciprocal relationships. So we'll establish clear
20 expectations of the roles and decision-making
21 authority of all partners. We will foster a co-
22 learning environment where researchers and

1 stakeholders understand one another's needs and share
2 ownership of research activities. We will develop a
3 partnership with our stakeholders by showing that we
4 value and respect the time and contribution of all of
5 our stakeholders, and we're committed to diversity and
6 inclusion. And then also, we will emphasize trust,
7 honesty and transparency through collaborative
8 decision making and information sharing.

9 In order to achieve these goals and to
10 follow these standards, we will evaluate the
11 engagement process throughout this project in order to
12 maximize contributions from all stakeholders. To do
13 this, we will use in-house data collection tools to
14 document stakeholder participation and contribution.
15 Right now, we're looking at using Microsoft Teams and
16 we're learning about all of the functionality for
17 managing that, and I think that that's going to be a
18 good opportunity to get some involvement of all of our
19 stakeholders and some communication.

20 Collect feedback on engagement using
21 brief surveys following each stakeholder meeting. And
22 then quarterly, the team and stakeholder

1 representatives will review the data, and then discuss
2 whether any modifications need to be made and then
3 implementing those.

4 So now we're moving into the UH-3. For
5 UH-3, of course, there's a lot of planning that's
6 going on in the first two years. But currently, the
7 plan is to produce a physical function patient-
8 reported outcome measure from mixed methods research
9 and the PROMIS physical function item bank, which will
10 include three short forms for mild, moderate and
11 severe physical function impairment and a full-range
12 physical function form.

13 The second AIM is to produce a physical
14 function outcome or performance outcome measure
15 derived from the NIH Toolbox and the SPVB that's
16 optimized for responsiveness to conditions that affect
17 physical function.

18 And then the final AIM of UH-3 is to
19 validate the physical function pro and performance
20 outcome and three longitudinal studies: one that
21 addresses mild or moderate physical function
22 impairment, another that addresses moderate or severe,

1 and then one that addresses the full range of physical
2 function impairment.

3 So generally our expected approach is
4 that this will involve mixed methods. The qualitative
5 aspects will involve concept elicitation interviews
6 with patients in each of the final six selected
7 conditions, development of conceptual models, and
8 cognitive interviews of selected items or preexisting
9 measures. We'll also incorporate mixed methods in the
10 short form development. We plan to look at
11 calibrations, because these are existing item banks,
12 so that it can help inform some item selection
13 throughout that process.

14 And then finally, we will evaluate the
15 pro instruments and performance outcomes through
16 quantitative means using IRT calibrations and
17 validation studies.

18 Does anyone have any questions? The
19 webcast?

20 MEENA SAVANI: We do have some webcast
21 questions. And in the meantime, the audience members
22 are also free to walk up to the mic so we can rotate

1 back and forth. The question: are the PIs of these
2 grants collaborating at all with the Critical Path
3 Institute, or are they completely independent?

4 SARA SHAUNFIELD: I can't speak for the
5 other grants. But for ours in particular, we have two
6 representatives, Stephen Koons and Sonya Eremenco,
7 from the Critical Path Institute as our stakeholder
8 group.

9 MEENA SAVANI: Thank you. And another
10 question: how are you planning to assess saturation?
11 Three interviews per condition is a very small sample
12 size.

13 SARA SHAUNFIELD: I agree. So given
14 the scope of the work and looking at the conditions,
15 these aren't intended to be concepts elicitation
16 interviews. Essentially, we are just trying to get a
17 sense of the severity of the physical function
18 limitations, the importance to quality of life of
19 those different limitations, and the types of
20 limitations experienced, upper extremity and mobility,
21 so that this can help to inform those decisions in
22 selecting those six conditions.

1 And once we have selected those six
2 conditions, we will conduct up to 21 interviews until
3 we've reached saturation, and we define saturation as
4 conducting interviews until no new concepts have
5 emerged over three consecutive interviews.

6 MEENA SAVANI: Another question related
7 to sampling. With regards to the sample of 33
8 patients across six conditions, could you comment on
9 how this is going to reflect the principal of sample
10 representation to be able to generalize the findings
11 as described in the draft PFDD Guidance 1.

12 SARA SHAUNFIELD: That's a very good
13 question. I would -- so I would say with such a small
14 sample size, we can't get -- obviously cannot get a
15 diverse population. We're, again, just trying to get
16 a range of the physical function impacts and
17 severities. And I welcome any members of my team to
18 add to my response, and we can also get back to you on
19 that question.

20 WOMAN: So since sampling
21 representativeness is dear to my heart. I think,
22 though, that there's -- we're not going to have

1 prefect versus if you only have people that are only
2 at Northwestern University and they're all white and
3 they are all upper middle class or upper class. Like,
4 there's ways to have representativeness. And so, is
5 that, like, kind of how are you reaching out to try to
6 have some diversity, even though it may not, you know,
7 it's not going to look like the CDC national health
8 interview survey.

9 SARA SHAUNFIELD: And we're talking
10 about the scoping interviews --

11 WOMAN: Yes.

12 SARA SHAUNFIELD: -- not the concept
13 solicitation? So I think this is a really good point
14 that you've raised because, again, three interviews is
15 a very small number. But we are working with NORD, so
16 I think this is something important for us to consider
17 to get a diverse, or as diverse as we can. Through
18 initial aspects of literature, we can identify aspects
19 of the population that would be important to sample in
20 this very small sample. And then once we've selected
21 conditions, we can certainly expound upon that for the
22 concept solicitation interviews in the second phase.

1 Any other questions?

2 STEPHEN COONS: Stephen Coons from the
3 Critical Path Institute. And I didn't seed that
4 question, by any means, about the interaction with the
5 Critical Path Institute, but I'm the executive
6 director of the patient-reported outcome consortium.
7 But also, we recently got a seed grant from FDA to
8 establish a rare disease clinical outcome assessment
9 consortium.

10 And one of the things that we're trying
11 to do in that consortium, or will be doing once it's
12 established, is identifying measures that are at the
13 domain level for the most part -- physical function,
14 pain, fatigue, et cetera -- where peritus, which is a
15 symptom, but an important one across a variety of rare
16 diseases, and we are very interested in collaborating,
17 obviously, with this initiative at Northwestern. And
18 certainly Bryce and his team work in pain in infants
19 because so many of the rare diseases that we're going
20 to be dealing with do involve infants and children.

21 So the point is, there's a lot of
22 interaction with these groups and will be in the

1 future, so I want to just assure everyone that CPATH,
2 the Critical Path Institute, is very much wanting to
3 collaborate and willing to collaborate and has
4 discussion collaborations regarding what is being done
5 in these three studies specifically. Not much in the
6 migraine area at this point because that's very
7 specific to that disease, but we are interested very
8 much, particularly in the Northwestern and Duke
9 initiative.

10 Well, physical function, yes, is
11 certainly one. But I mentioned peritus because that
12 has come up as an important area within rare diseases.
13 But, yes, physical function, fatigue, a number of
14 domains that will be useful to assess across multiple
15 rare diseases. The problem is there are 6,000 to
16 7,000 rare diseases, and we can't have disease-
17 specific measures for every one of those diseases. So
18 we have to find measures that could be used across
19 multiple diseases as endpoint measures in clinical
20 trials, so it's one of the things we're going to be
21 working on.

22 SARA SHAUNFIELD: Thank you for that.

1 Are there any other questions?

2 MEENA SAVANI: A question from the
3 webcast. As it relates to the model conditions in AIM
4 two of UG-3, could the most common cause of physical
5 limitation in the U.S., obesity, also be included? It
6 seems to be a missed opportunity to not assess this
7 condition that impacts over a third of the U.S.
8 population. Thank you for considering addition of
9 obesity as a potential model condition.

10 SARA SHAUNFIELD: You know, honestly, I
11 thank you for your comment and your question. I think
12 -- I hadn't even considered obesity. I think that's a
13 really important in terms of physical function. I
14 think that I wouldn't be able to make that decision
15 here, but I would need to confer with my team, but we
16 can certainly have those discussions.

17 MEENA SAVANI: Another question: why
18 focus on sarcopenia?

19 SARA SHAUNFIELD: The sarcopenia is
20 something that's experience -- will eventually be
21 experienced by every one of us in terms of aging, and
22 it's also associated with a lot of chronic conditions.

1 Sarcopenia is something that isn't well defined, which
2 creates a lot of challenge for us in this space and
3 that we'll be figuring out as we go. And there's a
4 lot of discussion on what constitutes sarcopenia, how
5 do you measure it. And it is an important physical
6 outcome and it's important for these conditions that
7 are undergoing regulatory review, and important for
8 new drugs and new treatments to be developed. So we
9 hope that we're on the cutting edge of helping to move
10 this effort forward.

11 ROBYN BENT: Thank you.

12 SARA SHAUNFIELD: Thank you.

13 ROBYN BENT: Okay, thank you so much,
14 Dr. Shaunfield. We are not going to take a 15-minute
15 break and reconvene at 10:15. Thank you.

16 (Break)

17 ROBYN BENT: And at this point, I'll
18 just ask all panelists to come up to the panel. Okay,
19 welcome back. I hope everybody enjoyed the break.
20 And we're going to add -- just before we start with
21 the panel presentation, we're just going to add a
22 small plug for people to submit any feedback or

1 comments to the public docket, which is open until
2 January 6th.

3 And now, we're going to move on to the
4 panel discussion. We are fortunate today to be joined
5 by several members of the FDA staff, a representative
6 from each one of our grantee teams, and one of our
7 patient experts. At this time, I'm going to ask each
8 of the panel participants to provide a brief
9 introduction of themselves before we launch into the
10 panel discussion.

11 Please note that at the end of the
12 panel discussion, we've reserved approximately 20
13 minutes for questions from the audience, both in the
14 room and online. Thank you.

15 KANECIA ZIMMERMAN: I'm Kanecia
16 Zimmerman from the COA-APTIC team at Duke.

17 HEATHER BENZ: Heather Benz, Center for
18 Biologics Evaluation and Research.

19 KATIE GOLDEN: Good morning, my name is
20 Katie Golden. I'm a patient advocate living with
21 chronic migraine disease.

22 LAURA LEE JOHNSON: I'm Laura Lee

1 Johnson and I'm in the Office of Biostatistics in the
2 Center for Drug Evaluation and Research.

3 ELEKTRA PAPADOPOULOS: Good morning.
4 I'm Elektra Papadopoulos, and I lead the Division of
5 Clinical Outcome Assessments and Office of New Drugs,
6 CDER.

7 DEVIN PEIPERT: Devin Peipert from
8 Northwestern University, representing the NUCOAT team.

9 MICHELLE TARVER: I am Michelle Tarver.
10 I'm the Director of Patience Science and Engagement at
11 the Center for Devices and Radiological Health.

12 R.J. WIRTH: Hi, I'm R.J. Wirth. I'm
13 one of the PIs for the MiCOA project, as well as
14 managing partner of Vector Psychometric Group.

15 ROBYN BENT: Wonderful. Thank you very
16 much. To kick our questions off, I'm going to start
17 with what I hope to be an easy question, which is
18 directed mostly to the grantees. But I'd also really
19 be interested in feedback from Katie as far as why did
20 you want to be part of this program for the grantees,
21 why did you apply. And maybe you wouldn't mind
22 starting, R.J.?

1 R.J. WIRTH: Happy to. It is a simple
2 question, I think, but it's -- I don't know how we
3 could not have wanted to be part of the program. You
4 know, as Richard mentioned earlier during his
5 presentation, migraine is such a impactful disease.
6 You know, not just the number of people that
7 experience it; it's the degree in which it impacts
8 peoples' lives. And, you know, so many people are
9 affected to the point where, you know, it's hard to
10 work, it impacts your social life, whether or not they
11 can go to their, you know, kid's wedding becomes an
12 issue.

13 And while there's a lot of interest and
14 new treatments and currently, it seems like it's sort
15 of a prime time in migraine, right? There's a lot of
16 interest in new treatment. There really hasn't been,
17 in recent years, a ton of new work in endpoints and
18 outcomes. And we've been talking about it now for,
19 you know, a couple of years at least, if not more,
20 about how nice it would be to have the time and the
21 resources to dig in and really explore what's out
22 there and understand what's out there. And while

1 there are some new developments, you know, try to
2 better understand what's being developed.

3 And when we saw this opportunity come
4 by, and especially when it mentioned migraine
5 specifically in the RFP, we just -- we thought, you
6 know, we had to do this. And, thankfully, FDA agreed
7 or else it would have been very awkward with me coming
8 up here to talk otherwise. But, I mean, it really was
9 just something, that we think there's a real need.
10 And if we're thoughtful and, you know, with the team
11 that we have put together and with the collaboration
12 at FDA, hopefully, we can make a real impact on this
13 industry and, hopefully, help patients, so I think we
14 had to do it.

15 DEVIN PEIPERT: It's Devin from the
16 NUCOAT team here. I think one thing, you know, that
17 we responded to specifically was the opportunity to
18 locate a thru-line across a number of, you know,
19 potentially diverse but also, you know, similar
20 conditions and find a way to measure important
21 outcomes across those.

22 So we've, you know, our team works a

1 lot with PROMIS and Neuro-QoL and Toolbox and
2 measurement systems that address a number of chronic
3 conditions and we feel that are appropriate in that
4 there really is a commonality across some of those
5 conditions that can be measured very well. And this
6 was an opportunity to leverage that to the benefit,
7 you know, we think of industry, of patients and
8 regulators to help systematize and bring together, you
9 know, using the efforts that went into all those
10 measurement systems through the, you know, the NIH
11 funding and other sources that went into those.

12 KANECIA ZIMMERMAN: So I'm a pediatric
13 intensivist, also a clinical trialist. And as a
14 clinical trialist, children are so often forgotten,
15 and that's the reason I want to be a clinical
16 trialist, because I feel like we really have to kind
17 of fill those holes. And a lot of the time, children
18 are so often forgotten because it's hard, it's really
19 difficult, and I think I mentioned that earlier.

20 And one of the reasons that things are
21 difficult is because we don't have the right tools to
22 be able to actually measure things, and that was

1 really a motivating factor. As a pediatric
2 intensivist standing at the bedside of a child and not
3 really knowing what's happening or how I should be
4 treating them, it's frustrating. And it's frustrating
5 to me as a clinician, it's frustrating to parents, and
6 that really is the motivation -- my motivation and
7 certainly for moving forward.

8 I'm thrilled to have a team who can
9 help me and partner to be able to measure things and
10 to apply the correct methodology to make sure that we
11 can do this correctly.

12 KATIE GOLDEN: I have to say thank you.
13 The reason I put my sunglasses on is because the
14 screens right here and the background is white. And
15 actually, that's something for everybody who is
16 working on one of these grants, especially for
17 migraine. That hurt my eyes and it could induce an
18 attack, so thank you that was recognized. I really
19 appreciate it, and I might stay movie star style for a
20 little while longer. But that is part of my everyday
21 life and I'm not the only one.

22 So I had an episodic migraine with

1 aura. My first attack was when I was 5 years old, and
2 I was episodic, meaning clinical definition 15 days a
3 month, headache days a month or less -- or 14 or less.
4 And right before my 30th birthday, I had a migraine
5 attack as normal, as there was nothing different about
6 it, except that it never stopped. And I was the
7 youngest vice president in my company in commercial
8 real estate financing, and I eventually had to stop
9 working because the migraine still has not stopped.

10 It's a disease, and it's on such a
11 wide, wide spectrum. So whether or not you have it or
12 you know somebody who has it, what they experience and
13 what I experience can be extremely different. And so,
14 I'm sitting here telling you that I have -- in eight,
15 almost nine years -- I have not had a pain-free
16 moment. And you might not believe me because I'm
17 wearing movie star sunglasses and, you know, I've
18 curled my hair and I put my makeup on and I put a
19 dress on, you know, I look decent.

20 But I think just in general, when you
21 think about disability, I don't look like I'm
22 disabled. The government has agreed with me that I am

1 disabled. And some of the things, especially with the
2 study on children, you know, they can't verbalize it.
3 You may not be able to see it, the pain that they
4 have. And so, invisible illnesses and, for me,
5 getting the public to understand.

6 And then also, I'm just excited that
7 NIH and FDA is also interested in, with the public, in
8 making changes. And in doing so and including the
9 patient voice, I think that the public will get that
10 so many people are walking around, you know. There
11 could be -- I'm sure that there are a lot of you right
12 now who have chronic pain and I couldn't tell. But it
13 is extremely disabling, and I'm just excited for the
14 opportunity to share and, hopefully, we all can learn
15 from each other. Thanks.

16 ROBYN BENT: Thank you. And actually,
17 I think moving on, I think you've kind of touched on
18 it, but I'm going to ask you maybe a direct question
19 about why would -- like, in your opinion, why would
20 patients want core outcome sets; what benefits do you
21 think they could potentially have patients?

22 KATIE GOLDEN: I like visuals,

1 especially -- yeah, so this this bag here has all of
2 my medications in it. And that includes for migraine,
3 it includes rescue medications, so when my attacks get
4 really, really bad, I can take. It's also
5 preventative medications. It also includes vitamins
6 and supplements and extra -- so there's a lot of
7 different stuff in there. And it not only includes
8 oral tablets, but it also includes syringes and glass
9 vials that I have to break and get shots to give to
10 myself.

11 So my point in showing you this -- and
12 it's rather heavy -- I have to travel with this. And
13 if I'm -- I mean, I'm staying at a hotel nearby, but I
14 may need something in this during this meeting. So
15 the real point is that I think all patients don't want
16 -- we would love to be able to lighten this load. And
17 so, if we can change the clinical outcomes so that
18 they are geared to what patients care about, you know.
19 This is just an extreme example, like, we don't want
20 to take all of these, you know? I don't think any
21 patient does. I can elaborate, but that is just one
22 thing. That if follow-up questions, please feel free.

1 ELEKTRA PAPADOPOULOS: Sorry. I just
2 wanted to say how much we appreciate your involvement
3 and these efforts and the patient perspective is so
4 critical. And I think some other things that we often
5 hear from patients are that the clinical trial
6 eligibility criteria can be very restrictive. And,
7 you know, to have outcome assessment that could be
8 potentially applicable to broader population. I mean,
9 you mentioned that you have continual pain. And so,
10 you know, it's --

11 KATIE GOLDEN: So to that point in
12 particular. Yes, I've never been part of a clinical
13 trial because there are so many. And, you know, I
14 understand, you know, having the controlled studies;
15 they're necessary to make sure that whatever treatment
16 you're working on that, you know, you get the pure
17 unbiased outcome that you need.

18 However, the real world, you know,
19 there's a new class of medications for prevention of
20 migraine that came out last year. And, you know, it's
21 not required of the pharma companies or, you know, in
22 FDA approval process -- correct me if I'm wrong --

1 that, you know, the real-world case studies of how a
2 new drug will interact with something that I'm already
3 taking.

4 For instance, if I'm taking a new CGRP
5 inhibitor medication and I'm also using Botox for
6 prevention of migraine, there weren't studies done on
7 that. And so, there were some healthcare providers
8 who were comfortable with just adding it on, adding
9 the new CGRP on, and then many said, no, you can only
10 do one or the other, and then insurance companies
11 decided also, you can do one or the other.

12 So that is something that I, and many
13 other patients, have experienced and that's really,
14 really frustrating. And so, the real-world evidence,
15 it really is important, you know. I know that the
16 process to get to approval is very long. But for
17 patients, a lot of women who are pregnant who have
18 chronic migraine while they're pregnant, and we don't
19 totally know yet if that's -- you know, if there's a
20 risk there. And so, that's just one example of a
21 real-world bringing those two things together, and so
22 women are hesitant, as they should be.

1 But those are the kinds of things that
2 patients care about, outside of, hey, there's this
3 great new drug, that's awesome. And the label may say
4 the only side effects are constipation and injection
5 site irritation. Yet, I do know of other patients who
6 are on these medications, and hair is falling out,
7 they're having other abdominal pain and symptoms. And
8 that's because, you know, in the real world, they're
9 adding it on to and they have comorbidity. So, you
10 know, the amalgamation of all of these, plus something
11 new, plus their daily life isn't studied.

12 So that's something that is very
13 important because a lot of patients who aren't really
14 clued in and don't have support, the migraine
15 community is very large but very connected. But some
16 people in taking a brand-new medication, no matter
17 what disease area it is, that they will -- they might
18 say, oh, well, it's not listed. Is this side effect -
19 - is this a side effect, is this just something new,
20 am I crazy, do I even tell my doctor? So, yeah, I
21 mean, patients struggle with that, and I hope that
22 answers your question.

1 LAURA LEE JOHNSON: And I might work
2 off of that a little bit because actually a lot of
3 what you just said reminds of part of what we heard,
4 even thinking about the oncology community. And
5 actually, I think we have people from our Oncology
6 Center of Excellence who would answer this a little
7 bit better than I do, and they can correct me if I get
8 this wrong. But a lot of -- one reason that NIH had
9 built up the peer CTCIE, which was a patient-reported
10 set of actually systematically asking about adverse
11 events, and a lot of this really gets to tolerability.

12 And what they wanted to do is say, as
13 you're doing trials, like, you know, a lot of times in
14 many of these grants and the funding has been focused
15 on efficacy, but a lot of this is also safety and
16 understanding the tolerability. And right now, much
17 of that information outside of it, it was, like,
18 efficacy people have an idea, like, I need to have a
19 fixed way that I'm measuring this in everybody.

20 KATIE GOLDEN: It doesn't work that
21 way.

22 LAURA LEE JOHNSON: And it doesn't work

1 that way. But then there's the safety part is, you
2 know, the clinician decides to write it down during
3 the trial. And then we've got folks like our medical
4 officers, they're trying to sift through this and try
5 to decide is there a signal here that then goes on a
6 label that then your doctor looks at or you see it
7 online as you're trying to do and look about what
8 treatments do I have and what do I want to do.

9 And so, part of the good part of this
10 core outcome sets is to really say, okay, what is it
11 that at base we are going to try to measure. And the
12 goal would be to say, hopefully, trials would say
13 we've got something and now we can plug it in. We're
14 going to say, like, what it's good for. Maybe it
15 doesn't exactly for your product, but to say this is
16 already kind of -- we've got a lot of information,
17 we've got a lot of evidence, we've got a lot of
18 background.

19 Because right now, what happens many
20 times is each individual sponsor for their particular
21 molecule or what have you goes in, they have you sit
22 in front of those screens and there is all of these

1 panels and focus groups. And it's not that a new tool
2 and more development will never have to happen, but do
3 we have to redo it every single time for something
4 that is, in fact, pretty consistent.

5 And so, from an entire efficiency and
6 systems standpoint, that's part of what I think is
7 really beneficial of having those core outcome sets
8 and what we're looking for here, because we've heard
9 it from everybody -- from the patients, from the
10 sponsors, from lots of different groups. But it's
11 also to remember that many of these elements you've
12 brought up, like, that may be brought in.

13 And I think an important part of having
14 that patient involvement is, you know, the tools that
15 we learned and we held dear because people have used
16 them for the last 5, 10 or, in some cases, 75 years,
17 may not be what we should be using right now. And so,
18 where should we be moving forward?

19 KATIE GOLDEN: And another point to add
20 on to that is, in particular in the migraine area, we
21 have had experience where individual sponsors have,
22 within their individual drug development programs,

1 develop, you know, very similar tools. But really,
2 you know, what is the efficiency in that? And so,
3 that's part of the goal here is to have a uniform tool
4 that could be used across. Yet, and I recognize that
5 sometimes we do need to have individual, you know.
6 But where there's an opportunity to collaborate and to
7 have common tools where we can compare apples-to-
8 apples and have common metrics to really allow
9 informed decision making with prescribers and patients
10 and have intelligent choices there.

11 MICHELLE TARVER: If I could just chime
12 in really quickly. You know, we're talking about
13 drugs, but also in the device realm. I mean, there
14 are new challenges that exist in devices. And devices
15 are things that are implanted in patients, so there's
16 a different calculus that goes into determining, am I
17 going to take the risk of something that's
18 experimental and is going to stay with me potentially
19 for the rest of my life.

20 So how we assess safety in that context
21 is maybe different than how you do it for a drug. So
22 having a core set of outcomes that assesses one of

1 those concepts, it's also important for that
2 condition, allows industry to focus their efforts in
3 developing what may be the gap and filling that in,
4 instead of repeating the exact same thing over and
5 over again.

6 HEATHER BENZ: This is relevant for
7 biologics as well. We have a variety of rare
8 conditions that often show up with products,
9 conditions for pediatric patients, conditions with a
10 variety of adverse events. And particularly where
11 there are small patient populations, the patients are
12 begging for efficiency. You know, please tell the
13 sponsors that the trials will be quick and easy to
14 design so that they will do them.

15 So we see a real need for efficiency so
16 that patients have increased access, not only to
17 products already under development, but products that
18 are in the pipeline or that could be in the pipeline
19 were there enough efficiency.

20 ELEKTRA PAPADOPOULOS: That's a great
21 point, and that's true across the board. Lowering
22 some of those barriers for development is a key goal.

1 ROBYN BENT: Great, thank you. I think
2 we'll now move on to the next question because I want
3 to make sure that we get to it. And this one, I'm
4 going to kind of aim initially at you, Elektra. It
5 seems like there are a lot of efforts related to
6 clinical outcome assessments going on across CDER.
7 Can you talk a little bit about these efforts and how
8 they are similar and how they are different? And then
9 we'll move on after that to our representatives from
10 CDER and CDRH and ask them about their programs as
11 well. Thank you.

12 ELEKTRA PAPADOPOULOS: Certainly, and
13 thank you for that question; that's an important
14 question. And I think, you know, I'll give sort of a
15 long-winded question because I have to provide some
16 background. I know many of the people in the audience
17 are already familiar with some of these efforts.

18 But I first wanted to highlight the
19 drug development tool qualification effort and to
20 remind ourselves. Drug development tools are
21 materials, methods or measures that could potentially
22 facilitate drug development. And so, included in this

1 definition are, of course, clinical outcome
2 assessments, as well as biomarkers. We also have in
3 our program animal models for use under the animal
4 rule, but today, we're obviously going to focus on the
5 clinical outcome assessments.

6 So really, what is qualification? It's
7 a conclusion and it's based on a formal regulatory
8 process that, within a particular a particular context
9 and view, so it's very context specific, that the tool
10 can be relied upon to have a specific interpretation
11 and application in medical product development and
12 regulatory review.

13 And so, FDA has established
14 qualification programs to support drug development,
15 took development. And as we'll hear, the Center for
16 Biologics and CDER share programs, a joint program,
17 and CDRH, in addition, has a parallel qualification
18 program for medical device development tools.

19 And so, you know, we've heard expressed
20 very well earlier, you know, the goals of the core
21 clinical outcome assessment program, which is very
22 similar in that we want to have publicly available

1 tools, tools that can be used in clinical trials that
2 have been vetted with the agency and have buy-in from
3 plurality of stakeholders, and that can be used in
4 multi-national trials. So, you know, there are a lot
5 of, you know, common goals, and these programs are not
6 mutually exclusive and could really complement each
7 other very nicely.

8 But I also do want to emphasize some of
9 the differences between the programs. They are
10 distinct programmatically, so there are different
11 processes. The drug development tool program is a
12 well-established program; it's been in existence for
13 many years. And recently, with 21st Century Cures
14 Act, it has been formalized and is now part of our
15 mandate, and we also expect upcoming guidance
16 outlining the process of this qualification.

17 The core clinical outcome assessment
18 program, of course, as we've heard is in its infancy.
19 It's a pilot program and so, we're obviously still
20 learning. And it's also a grant program, so it's
21 different in funding. The drug development tool
22 program is not a grant program. And so, one of the

1 more content issues is that the core clinical outcome
2 assessment program is a little bit broader in focus;
3 it's focused more globally around comprehensive sets
4 of measures, as well as endpoints.

5 And these can be, as we've heard with
6 the case of migraine, in a particular disease area or,
7 in some cases and how we've defined it for the purpose
8 of this program, could cross-relevant disease areas
9 that share common domains, such as physical
10 functioning or certain symptoms. And so, you know, as
11 we discussed, this has great advantages also in
12 allowing us to, you know, compare across products of
13 similar classes potentially.

14 And so, you know, it's really our hope
15 and our goal that the tools and endpoints will be able
16 to satisfy multiple stakeholders because we know that
17 drug development is really multi-national. And it's
18 very important to also remember health technology
19 assessors in this process, and so, we need to pay very
20 close attention to tools that can be able to be
21 translated for multiple languages, as well as culture
22 groups. Consensus development in this regard is also

1 going to be very critical with the development of core
2 outcome sets. We need to have consensus on common
3 sets that can satisfy these stakeholders, and so we're
4 going to be pulling in a broad range of stakeholders,
5 as we've heard earlier.

6 The other key thing is, you know,
7 qualification is really focused on an individual tool,
8 so it's a tool that's for a particular context of use.
9 And so, each qualification project is associated with
10 only one tool, it's not a set of tools, and they are
11 important to fill these critical measurement gaps,
12 however. So before we take anything into the
13 qualification program, we ask ourselves, is there a
14 drug development need, is there an unmet need here,
15 and so that's very important.

16 But, you know, at the end of the day,
17 the measures and endpoints in both of these programs
18 need to be fit for purpose. And so, we're going to be
19 reviewing evidence in both cases, and the core
20 measurement principles are going to be applicable
21 across, so our standards are going to be maintained
22 with any of the measures coming out of these programs.

1 Both of these programs are voluntary.
2 So drug developers, rest assured, you will also -- we
3 will also continue to interact with you around
4 clinical outcome assessments within your individual
5 drug development programs. So that is also a key part
6 of our day job here at FDA.

7 So I just wanted to say in closing
8 that, you know, we envision that these two programs
9 will be complementary, not mutually exclusive, and
10 that the learnings can be applied across both because
11 measurement excellence is really shared across these
12 programs. Both programs will be looking to leverage
13 existing tools and learnings and not reinvent the
14 wheel, so those are very important.

15 We're very committed to the success of
16 each of these programs and the multidisciplinary
17 nature, so it's not only, you know, the measurement
18 folks, but clinical and biostats all coming together.
19 And we're committed to sustaining the programs and
20 maintaining them because it's not just about the
21 initial development, but also maintaining these over
22 time.

1 And so, finally, you know, really our
2 ultimate goal is the sustainable incorporation of
3 patient voice in clinical outcome assessment and drug
4 development. And so, I think that sort of recaps the
5 key features of our efforts.

6 ROBYN BENT: KATIE GOLDEN: Thank you.

7 KATIE GOLDEN: Is it okay if I just
8 very quickly mention something?

9 ROBYN BENT: All right.

10 KATIE GOLDEN: And also before I do
11 that, is it okay, because the patient community lives
12 online -- is it okay, I've got my phone here for me to
13 hit go live. They'll just see me, and I've redirected
14 them to watch this. If I can't, that's totally okay.
15 I'm trying to get more patients to watch because this
16 is really -- a lot of us are very, very excited about
17 this.

18 ROBYN BENT: I think you can go ahead
19 and try it. If we find that there's any sort of
20 interference or something like that.

21 KATIE GOLDEN: Oh, sure.

22 ROBYN BENT: And it's also streaming

1 live for you as well.

2 KATIE GOLDEN: Sometimes when they go
3 live, I've got the link for them to watch the whole
4 thing so I can probably do it in a few minutes.
5 Because I know you guys care, I mean, I'm here as a
6 patient, but there are so many that could be here
7 right now and could say the exact same thing.

8 I want to mention to your point, you
9 mentioned having -- trying to find a tool that kind of
10 works, and I wanted to clarify. Finding a clinical
11 outcome tool that -- you were specifically saying that
12 about for each disease area or across all disease
13 areas. Can you clarify that for me?

14 ELEKTRA PAPADOPOULOS: Okay, yes. So
15 in the case of migraine, the goal is to identify a set
16 within the disease area of migraine. And however, you
17 know, for the purpose of this grant, we've also
18 expressed interest in tools that could be used to
19 measure common symptoms or impacts or functioning that
20 span across disease areas.

21 KATIE GOLDEN: So I will -- thank you
22 for the clarification, so that I make sure my comments

1 are germane to this.

2 KATIE GOLDEN: Thank you for the
3 clarification so that I make sure that my comments are
4 germane to this. And so, you may want to think about
5 starting with -- there are a ton of, you know, apps
6 that you can use, that patients use, that you could
7 look at, and there are lots of patients who have also,
8 you know, kept daily diaries. And their input earlier
9 on probably is going to save a lot of heartache and a
10 lot of frustration.

11 And this isn't just for migraine, you
12 know, and the other areas as well, because I just
13 recently had a conversation, and somebody mentioned
14 just, how were you in the last, you know, seven days
15 or the month? And keeping a headache diary or using
16 an app, that screen time, that can be difficult. Or,
17 like, if you're having a really horrible attack, I
18 can't go into -- you know, technology is great, but I
19 can't do this. And if it's 30 questions that I need
20 to answer once a week or once a day, you're not going
21 to get the information that you need. There are
22 probably some other ways to get the information that

1 you need, and so I would just suggest to everybody,
2 like, you kind of start with them as well -- start
3 with patients instead of building it first.

4 MICHELLE TARVER: So, this is Michelle.
5 I think that, you know, your point is very well
6 founded. I mean, I think that a concern that we have,
7 especially as we're moving into an era where we're
8 using more real-world data to inform our regulatory
9 decisions as well as integrating that information into
10 our healthcare plans -- I'm a clinician as well --
11 it's important that we deliver tools to patients that
12 are going to be completed. Otherwise, missing data is
13 not useful data, no matter how well developed a tool
14 is. So, I think a pragmatic approach to integration
15 of that information is absolutely spot on.

16 Also, to your point about apps, there's
17 a lot of work happening. Our center works on mobile
18 applications, as well as other digital health
19 technologies, and how do we best capture other pieces
20 of information that may be complementary, that reflect
21 how a patient is feeling and functioning? I think
22 that is really a critical space when a patient cannot

1 report, I think both for the pediatric situation as
2 well as for somebody in the middle of a crisis. How
3 do you collect information about that in real time?
4 And I think that there's a lot of work and interest in
5 exploring that, so I do think that you bring up kind
6 of that next horizon. Where do we go next?

7 I think for the CORE grant, I think
8 it's critical to our efforts. We have not only a
9 guidance document that's been final for a number of
10 years about using real-world data as real-world
11 evidence in regulatory decision making, and using that
12 information to expand our label indications, as well
13 as for premarket and post-market monitoring of medical
14 devices. We want to make sure we get the patient
15 perspective, but what we've been seeing is that the
16 questionnaires are too long. They're too difficult to
17 collect, so we can't incorporate it into our
18 regulatory decision making.

19 And developing core outcomes that are
20 pragmatic and practical will help us have a better
21 understanding over the total product lifecycle of
22 medical devices, as well as biologics and drugs.

1 R.J. WIRTH: And, could I just build on
2 that for a moment? While it's not a goal,
3 necessarily, of this grant process, and you know,
4 we've had a lot of conversations already within our
5 team about how important it is for what's being
6 developed here, if possible, to be able to port that
7 into other arenas so it can be used in, you know,
8 within clinics. It can be used in other areas to get
9 us not just on a common metric, but if we can use, if
10 not the exact same tool, having some sort of linking,
11 some sort of system that will allow us to easily
12 incorporate real-world data, allow us to easily
13 incorporate data directly from the clinic and have a
14 better understanding -- you know, with regard to some
15 of the points that came up earlier -- have a better
16 understanding about, you know, what types of
17 interactions are occurring; have a better
18 understanding of how people are feeling when they're
19 not in this very structured clinical trial.

20 So, while I know it wasn't the goal of
21 the granting process, you know, I hope we're -- and
22 knowing the other teams, I'm sure we are all thinking

1 about not just what can we do for clinical trials, but
2 how can we build something that's useful outside of
3 the clinical trial to allow us to have a better
4 understanding of just patient experience across the
5 board.

6 LAURA LEE JOHNSON: And I also want to
7 bring up to the point, because hopefully -- I'm glad
8 that we are recording this, because this is our plan
9 language summary now for guidance to -- of the
10 guidance series. Which, in many ways, part of what
11 we've been trying to talk about, and I was glad that
12 Michelle mentioned the 2009 final PRO guidance that
13 her center, Heather's, and then our center all signed
14 onto. And we all say, at the core, you start with the
15 patient. Don't develop something and then throw it at
16 them, just get some math off of it, and you're done.

17 But I think the important part that
18 also, to reiterate, we've been saying like, what novel
19 ways could you collect information? And, you know, I
20 know for years, I put every single thing that I ate
21 and drank into one of those apps. And so, that's
22 information that can then be leveraged, and then other

1 folks that are doing other types of daily diaries,
2 does it take a lot more work to go through those
3 transcripts and more free-flowing information? It
4 could.

5 But also, sometimes that's where we are
6 in order to try to do and leverage information,
7 especially if you're thinking about, hey, I need to go
8 talk to FDA and say that the fact that people need to
9 answer within -- or talk within your own company -- we
10 need everybody to answer this questionnaire within a
11 two-hour window. Well, for our disease, that's not
12 going to work. Here's the justification for the
13 window. You now are bringing in that evidence to
14 provide that justification.

15 So, there are a lot of ways to
16 creatively leverage information, not only in the core
17 outcome arena, but also in trying to really define and
18 set up clinical trials that are going to be useful and
19 feasible at the end of the day.

20 DEVIN PEIPERT: Yeah, I'd like to just
21 add that, you know, our team from NUCORE couldn't
22 agree more. I think even looking at something like

1 the concept of physical function, it may be one of the
2 sort of core health concepts that we think we
3 understand very well, but those of you who heard Sarah
4 from our team talk earlier heard that we're going to
5 be doing a great deal of qualitative work. And, even
6 though I'm a quantitative researcher, I'm on the math
7 part, I'm probably most excited about that element
8 because I think it's going to give us the opportunity
9 to look at, across this range of conditions, what's
10 the common element that can be measured well from the
11 patients' perspective that's a good therapeutic target
12 in that area, and then push that into the measures.
13 And we know how to do that, but I think there's going
14 to be a lot of new knowledge coming out there, which
15 should be very exciting for everyone.

16 ROBYN BENT: Great, thank you very
17 much. I'm going to bring the question -- I think this
18 was a really, really great conversation. I'm just
19 going to bring us back a little bit to hearing about
20 the different efforts that CBER and CDRH have work
21 going in the COA realm. And so, I don't know if --
22 Heather, do you want to start?

1 HEATHER BENZ: Sure, thank you. So, in
2 CBER, we do partner with CDRH and do leverage the
3 qualified Drug Development Tools and other ongoing
4 programs there.

5 So, in addition, we have funded a
6 number of studies related to COA development, with the
7 goals of helping those patients with rare diseases and
8 rare pediatric diseases that I mentioned earlier.
9 They include research aimed at improving our design of
10 clinical trials so that, for rare diseases, maybe you
11 don't need as many patients in the control arm if we
12 can have ongoing natural history studies with robust,
13 built-in COAs. We're demonstrating that project with
14 NORD, the National Organization for Rare Disorders.

15 We're also working closely with IBM to
16 build COAs into apps and into our ability to use a
17 variety of real-world evidence collected from a
18 variety of data partners across the U.S. It's
19 important for us to include the patient perspective in
20 that data to provide context and to elevate the
21 patient voice any time we're looking at safety data.

22 And then, we've heard a little bit

1 about pain and function here. There have been a
2 number of challenges for products that are intended to
3 alleviate pain and improve function, and we're
4 conducting research intended to improve our
5 understanding of how those interact, and also, improve
6 our understanding of what matters to patients about
7 that dual axis of pain and function, so that when we
8 see products, for example, that alleviate pain but may
9 not meet their endpoint on function, how do we
10 consider that, and how would patients with relevant
11 disorders ask us to consider that?

12 KATIE GOLDEN: Could I make a comment?
13 And, please, if I talk too much and we're short on
14 time, please tell me to stop. But just for something
15 for everybody to kind of think of is you brought up
16 the function and the disability and the daily burden.
17 Every disease area has their own set of issues and
18 daily things that they have to deal with. Just, I
19 think that I'm here so that I can kind of give a
20 better picture, at least in my experience with my
21 disease and my comorbidities, of what my day is
22 actually like.

1 So, I'm trying to be very short. I
2 think the general public thinks, oh, you have a
3 migraine. It's just like a hangover. Take Tylenol
4 and you'll be fine or -- sorry, shouldn't name brand
5 names, but you all know what I mean. And, you know,
6 if you don't have migraine or you don't know somebody
7 who does, hasn't seen somebody go through that, you
8 don't really understand.

9 So, in my absolute worst, worst day, I
10 will go -- actually, I will describe a flareup, as I
11 would call it, that I had last year. I didn't leave
12 my apartment, even to go to the lobby to get my mail,
13 for a month. Luckily, my amazing partner in my life
14 and the love of my life, he is also the head of CHAMP,
15 the Coalition for Headache and Migraine Patients. He
16 doesn't have migraine, but I was episodic when we met
17 and became chronic, daily, over that time.

18 So, something like that, I mean, I'm
19 lucky that he was supportive and I had that. He was
20 able to go do the grocery shopping and go downstairs
21 and get the mail. And it's not just about being, oh,
22 I'm nauseous, oh, there's head pain, I'm sensitive to

1 light and sound. It's so much more than that, and I'm
2 going to get real, and I'm going to be graphic,
3 because I think just in general, the public doesn't
4 realize this. And I think also, just in all the
5 disease areas, that you have to understand the daily
6 life.

7 So, you know, I could be puking all day
8 long. I could get numbness and tingling in my
9 fingers, and so I can't write. Or, sometimes I'm able
10 to look on a screen, and other times, just even the
11 thought of looking at it is horrible, even if I'm not
12 having a flareup. And some of the other things are
13 the cognitive impairment. I'm definitely, you don't
14 know me, but I'm definitely pausing right now because
15 I'm trying to find the exact right words to convey
16 what I'm saying, and I may totally blank on something
17 during this.

18 That's my daily life, and it's not just
19 me. While you're having an attack, that can be the
20 case. Or, if you are chronic, which actually, it's
21 estimated about 4 million Americans are considered
22 chronic, where they have 15 or more headache days a

1 month.

2 And the ability to work, or not work
3 actually, we all try to kind of -- I just grin and
4 bear it and work through it, because we want to do the
5 best job that we absolutely can. But, you know,
6 employers don't always get that. The fluorescent
7 lights that I see every day, I need accommodations.
8 So, either I can wear sunglasses, or we need to ask to
9 have a policy in place where people don't wear perfume
10 or cologne, because the smell of that can -- you know,
11 certain smells, and everybody is different with the
12 smells -- that's going to cause something.

13 So, there's things that you may be
14 doing that you don't even realize can hurt somebody
15 that you're coming in contact with. So, I think that,
16 yeah, I'll stop there, because I will ramble when I
17 can't find my words, so cut me off.

18 ROBYN BENT: No, but think it's really
19 important to hear from you, and I think that that
20 really kind of emphasizes the importance of the
21 qualitative research, to make sure that we're
22 measuring the things that really matter to you, and

1 not the things that we think matter to you, that we're
2 hearing from people. So, I think that it's very
3 helpful to just kind of reinforce that we're kind of
4 starting down what I think is a good path. And I know
5 that as you provide feedback for the COAs and stuff, I
6 think it's certainly clear that your participation is
7 going to add strength to the process, so thank you.

8 And now, I'd like to just to Michelle
9 to hear about the CDRH efforts underway. Thank you.

10 MICHELLE TARVER: Sure. And so, I
11 think I've already alluded a little bit to how devices
12 are different in terms of the level of invasiveness,
13 as well as what they are targeting to do. We have a
14 lot of research efforts also underway. Our focus has
15 really been on the safety aspect for multiple devices,
16 because surgery, in and of itself, is one thing, but
17 the actual device being in place elicits some
18 challenges, as well as gives some opportunities for
19 patients that may not have been available with other
20 treatments.

21 And so, we've got some work that we've
22 been doing, particularly in the ophthalmic space, that

1 we're excited about, because it's not just developing
2 a tool that can capture safety outcomes or how a
3 patient is living with their condition, but also using
4 different methodologic approaches to try to streamline
5 that process. And we've been taking advantage of
6 existing registry platforms. Right now, the IRIS
7 platform is probably the largest registry in the
8 United States. It sees about 40 million patients that
9 are housed in that registry with various medical
10 conditions, from the pediatric all the way to
11 conditions that affect our older adults. And in that
12 registry, they're using that as a sampling frame to
13 identify patients that we can do the validation and
14 work that's necessary to support a newly developed PRO
15 measure, identify them, and deploy. And our
16 clinicians are really excited about that in that
17 space, because they want something that they can
18 integrate into their clinical care, so we're exploring
19 how we can do that.

20 And I do think that's the new horizon.
21 As healthcare providers, I know increasingly, PRO
22 measures are being mentioned in preferred practice

1 guidelines. So, it's becoming part of our daily care
2 paradigms in many situations, for orthopedics, where
3 we look at physical function; for joint replacement
4 surgeries; or you're looking at intraocular lenses. I
5 can't always measure some aspects of it. I need you
6 to tell me the quality of the vision. And so, with
7 that in mind, we are funding research that can help
8 answer those questions.

9 The other thing we've been looking at
10 is in rare diseases, particularly things where the
11 tools we have currently bottom out. We can't measure
12 visual acuity in a patient who has light perception
13 vision. And I think this is something we have in
14 common with the biologics group, where we see new
15 tools or new treatments that are coming to market, or
16 want to come to market, but we don't have good ways to
17 measure how well they work. And so, not only are we
18 looking at just the patient-reported outcome measures,
19 but can we look at performance tasks that really do
20 simulate their real-world experience so that we can
21 see observable changes in that?

22 And so, we are working now with the

1 Foundation for Fighting Blindness, looking at
2 retinitis pigmentosa, which is a rare condition, and
3 figuring out ways that we can develop supportive
4 information to help support those tools and help
5 further device development processes, as well as I
6 know they have an intention as well for it to be used
7 in drug development programs as well.

8 And then, the last thing I'd like to
9 talk about is, while we've alluded to it a number of
10 different times, the digital health technology space
11 is really an exciting and new space, but it does
12 present some new challenges and questions that we
13 don't have great answers to right now. Our team has
14 been working. Our digital health is run out of our
15 center, and they've been working with lot of different
16 entities. We have a precertification program that is
17 a partnership, basically saying, we can't keep up with
18 the iterative cycles that happen with each app or
19 online tool, but can we at least have confidence in
20 the company that is providing those tools, and then
21 evaluating that in the post-market, how well it's
22 performing. But a lot of those tools incorporates PRO

1 measures as part of them, as well as sensor data and
2 other things, and integrate that. So, better
3 understanding how to do that, I think, is one of the
4 areas that we're also interested in looking at in our
5 center.

6 ROBYN BENT: That's great. That's
7 really exciting and I thank you for sharing that with
8 us, because I always feel like sometimes, I learn more
9 at these public meetings than I learn form our
10 internal meetings. I love to hear about things like
11 that.

12 I was wondering now if we could kind of
13 move into a little bit of a different sphere and maybe
14 start with a question for people who are actually
15 performing clinical trials. And I think that what I'd
16 really like to hear about, I think it would be helpful
17 to know is, if you've ever felt that you must use
18 multiple different COAs that measure similar concepts
19 in a clinical trial to satisfy different stakeholders,
20 such as payers, regulators, or clinicians. And, if
21 so, what are your thoughts on how this might be a more
22 efficient process, and how can the clinical outcome

1 assessment's core sets help.

2 KANECIA ZIMMERMAN: I'm happy to start.
3 So, the answer to your first question is, absolutely.
4 We've talked a lot here about feasibility. I think
5 almost every person on this panel has mentioned that
6 in the last couple of minutes. And we should also
7 think, really, about burden, burden on patients,
8 burden on families, burden on sites. Clinical trials
9 are extremely expensive. They are difficult to
10 conduct, and it is a privilege for us to be able to
11 conduct them and for people to be enrolled into our
12 trials. And so, we really need to be extremely
13 mindful about every step and every decision that we
14 make, particularly in special populations, be it
15 pediatrics or rare diseases, because we want those
16 people to come back for the next drug that we're
17 trying to evaluate, so we really, really need to be
18 mindful of that.

19 I think one of the ways that we might
20 be able to condense the multiple measures from
21 multiple stakeholders is rally to get upfront
22 consensus, which I think I'm happy, as a part of this

1 program, not only having our teams talk to the
2 stakeholders individually, but also having the
3 stakeholders talk to each other about the things that
4 really are important, knowing that we all are invested
5 in the same thing in the end, so how do we actually
6 get there?

7 KATIE GOLDEN: Something that you just
8 mentioned is making sure that you reach special
9 populations, and so I'm going to go just a little bit
10 further. Special populations, and I think you'd
11 probably agree, also means during clinical trials,
12 there are so many -- you need to try to have gender --
13 for migraine, there are actual gender differences in
14 how women and men experience migraine. You need to
15 have a wide range, depending on what it is you're
16 studying. Migraine is not just a middle-aged white
17 woman problem. Those are the women that actually seek
18 treatment, but those who don't -- you know, migraine
19 doesn't discriminate, so it is all age ranges, and it
20 does affect every race and ethnicity.

21 And there are also areas, rural areas
22 where, one, they may not have a doctor; two, if they

1 do want to and can participate in a clinical trial,
2 getting them to the site to actually be there,
3 actually I know that there's a few nonprofit
4 organizations that help bring patients to those sites.
5 But there are so many access barriers for patients
6 outside of what they're able -- sorry, the word --
7 exclusions. Outside of exclusions, there are a lot of
8 barriers for patients to participate. And they want
9 to, and so, just, yeah, think about it.

10 And actually, not just think about it;
11 it is incredibly important that their voices and their
12 -- that they're included. And I just want to say
13 thank you to -- I've not been in one, and thank you to
14 all the people that have. Because, you know, I
15 wouldn't be where I am today if people 30, 20, 10, 5
16 years ago weren't in a clinical trial. So, those
17 people are -- they're real people. They have real
18 stories, and they aren't a number. So, thanks to
19 everybody who's done that, and thank you all who are
20 in this field and doing this work, because I wouldn't
21 be where I am today if you guys collectively hadn't
22 pushed things forward. So, I'll leave it at that.

1 ROBYN BENT: Thank you. Did you want
2 to --

3 R.J. WIRTH: You know, obviously, as
4 sort of my role is often working with sponsors who are
5 making the ultimate decisions about what goes in, but
6 I do think we often see essentially multiple COAs
7 asking the same questions about the same constructs.
8 And I think part of it is the fear that, when the
9 trial's done, they don't want to have forgotten
10 something and go to an FDA meeting and say, oh, well,
11 do you have this particular thing? And they go, oh,
12 my God, now we need to do another study.

13 So, I think a lot of it's just sort of
14 unease with, or not having the confidence that when
15 they're done, they'll have everything they need. So,
16 I think in many ways, this program -- and, again,
17 what's different as opposed to a qualification
18 program, where we have a measure that, all right, well
19 you can feel confident about this measure, talking
20 about a set of endpoints and being able to walk into
21 and start a new trial, and understanding like, this
22 set of things is what people are going to want to see

1 at the end of the day. And if you have something else
2 that you're interested in, you could always add things
3 if you can justify the added burden on the patients
4 that are in your trial. But I think it will go a long
5 way in sort of easing concerns that we're forgetting
6 something.

7 So, I hope to see hopefully a lot less
8 redundancy moving forward, and hopefully, that will
9 make for more efficient clinical trials.

10 KATIE GOLDEN: Very quickly, R.J., I
11 think that people who are in clinical trials, they may
12 not get feedback after they're done. You know, did I
13 get a placebo? Once it's FDA approved or at some
14 point, you know, they invested a lot of their time
15 that they didn't have to. You know, you want
16 something out of them, but like, what do I get in
17 return? You know, I would want to know how I compared
18 to others, the other groups in the study. Did I get a
19 placebo? And it's also very hard when somebody's in a
20 trial and it is working for them, and then the trial
21 ends and they can't get that medication anymore unless
22 it is considered a lifesaving type of treatment. And

1 so, that is something that patients -- we want
2 feedback, and we want to feel like we are involved and
3 that our time is valued and it's not just one way.

4 ROBYN BENT: I think that's a very
5 valid point that I think definitely bears significant
6 consideration, because, I mean, I think all of us
7 would expect that patients are making a lot of effort
8 to participate in the trials, and we certainly
9 appreciate their efforts.

10 So, moving on maybe, unless anybody had
11 anything else to add for this question, I'd like to
12 move on to maybe the next question, which is, can
13 people on the panel discuss how core outcome sets can
14 be maintained and updated to reflect new information,
15 such as disease knowledge, measurement science, et
16 cetera?

17 DEVIN PEIPERT: Yeah, I'll go ahead and
18 start. So, I think one of the nice things about this
19 program in particular is, I know that every grantee is
20 enthusiastic about bringing in some of the updates in
21 our ability to measure patients' function, health,
22 pain, et cetera very well that have occurred, probably

1 since many of the COAs that are currently in trials
2 were developed. We've learned a lot about how to do
3 that, both in terms of efficiency, but as well as in
4 terms of creating flexible measures that can adapt
5 over time and can be added to or modified, as we learn
6 about diseases.

7 I'm thinking about things like item
8 response theory, which is a technical term, but it's
9 an approach that allows us to add in new information,
10 account for new information, expand the range of
11 people we can measure over time, without changing
12 fundamental or core aspects of the measures
13 themselves, so that you can add in that new element
14 over time when new information comes up. When you
15 bring it into the real-world space, you may need a
16 different level of physical functioning that you
17 wanted to measure in your trial, without necessarily
18 changing the underlying metric there and have scores
19 that are comparable, and a standard and a benchmark
20 that could be comparable over the course of time.

21 So, you know, the chance to bring that
22 into this environment and into trials is really

1 exciting and I think will be really beneficial. And
2 so, this is where I think we have an opportunity to
3 shine in that regard.

4 R.J. WIRTH: Yeah, and I think
5 something really nice about all three of the project
6 teams here is that -- and I'm just going to speak for
7 you. You know, I think we all sort of understand that
8 these assessment tools have shelf lives. I think for
9 a long time, somebody made something, you feel like,
10 okay, "it's validated." It's rubber stamped, and you
11 throw it out in the world, and it just goes forever,
12 and that's just not the way assessment works, right?

13 They need to be maintained. We need to
14 get new data. We need to make sure that, as the world
15 changes, and as people's interaction with the world
16 changes, that the assessments can also change with
17 them. And with the tools that are available and I
18 think the knowledge that are on all three teams, and
19 the experience that are on all three teams, we can
20 hopefully all develop assessments, or refine
21 assessments, that puts it within a framework in which
22 we can continually come back and sort of check in and

1 make sure that the assessments are behaving the way
2 that they were designed to behave, that are updated
3 when they need to be updated. And as our knowledge of
4 a disease, or as people's way, how they interact with
5 the world changes, that we can make those adjustments
6 without losing the ability to interpret those
7 measures, without losing the ability to have backwards
8 compatibility.

9 And, like I said, I think one of the
10 nicest things about -- you know, when I learned who
11 the other grantees were is that I know them, which is
12 nice, and I've worked with them before, and we've all
13 collaborated. And I think we all have an
14 understanding that, when we do this work, that it has
15 to be something that's sustainable and something we
16 can come back to.

17 How we do that, I think, is going to
18 depend a little bit on sort of what we're doing.
19 Hopefully, sponsors and users of the assessment tools
20 will be willing to share data, even if it's not
21 something we publish on, but to allow the scale
22 developers to go in and do this maintenance work and

1 make sure that we don't lose the precision that we're
2 developing from the tool. So, any sponsors out there,
3 keep that in mind.

4 KATIE GOLDEN: Just, very quickly, it's
5 a great point, R.J. I don't know how you exactly do
6 this, but for some diseases, it changes over your
7 lifetime. The way you experience it, for the patient,
8 changes. Your body changes, and so, you know,
9 chemical makeup -- and I'm not just talking about
10 women. Everybody ages, and so, if there's a way early
11 on to maybe include somehow those potential changes
12 and figuring that out -- yeah. So, I think you raise
13 a good point, and that's just kind of a nugget to
14 think about.

15 ROBYN BENT: Thank you. So, at this
16 point, we're going to move on to the audience
17 question-and-answer period. We had anticipated that
18 we would have lots and lots of audience questions, and
19 so we kind of broke the question-and-answer period up
20 first, so that if we had any patient stakeholders who
21 wanted to ask questions, we wanted to make sure that
22 we heard from them. So, at his point, if we have any

1 people who would self-identify as patient stakeholders
2 who would like to ask any questions, please feel free
3 to do so. Just come to one of the mics, either in the
4 center or on the side of the room. And then, once we
5 make it through the questions in the room, we'll turn
6 to the internet.

7 Okay, so we will turn to the internet.
8 Do we have any questions?

9 WOMAN 1: General Q&A.

10 ROBYN BENT: Okay, well, so it sounds
11 like we're going to move straight to the general
12 question-and-answer period, which is also wonderful.
13 And so, if anybody in the room has any questions for
14 our panelists, please feel free to come up to the
15 microphones now and share your questions. Or, if
16 you're feeling a little bit shy, we can start with the
17 web questions and then move on to the people in the
18 room.

19 KATIE GOLDEN: If you don't have
20 questions, while I was doing -- I'm still doing the
21 Facebook live, and so I have just one or two things
22 that patients who are watching this right now have

1 said.

2 One gentleman said, I can't watch much
3 longer because I'm in the middle of a seven-day
4 migraine and he has to go out to get medication
5 because he lives alone, and that's very, very painful
6 for him, especially right now. And so, that is daily
7 life. One, it was too long for him to be able to
8 watch on the screen. Two, he's got to go get a
9 medication, and it's extremely difficult for him to do
10 that.

11 And I felt like there was one other.
12 Let me just look real quick. Somebody else said that
13 it's been 12 years and has had a continuous migraine.
14 So, I just -- yeah, those two just really stood out.
15 So, if anybody on Facebook is still watching, I'll try
16 and look if you have questions as well.

17 MEENA SAVANI: Thank you for those
18 insights. So, from the web, the first question, the
19 COMET Initiative has a database published and ongoing
20 core outcome sets. One of the purposes of this
21 database is to avoid unnecessary duplication of
22 efforts for core outcome set developers. Have you

1 considered registering this work for COS developers?

2 And for FDA staff, would you recommend doing this?

3 R.J. WIRTH: This is R.J. from the
4 MiCOAs. We're aware of it and have had some very
5 brief interactions with that group. I don't think
6 we've made it far enough along in this process yet --
7 I mean, we're just a couple months into the project
8 itself -- to have a serious conversation about
9 registering. I think we first sort of want to get our
10 feet under us and get to a point in which we have a
11 better sense of where we're going to end up. And
12 then, from there, we'll hopefully have a little more
13 breathing room where we can sit down and have a better
14 understanding of sort of their role.

15 I'm not very familiar with their
16 organization, but it's obviously something that we'll
17 try to learn more about and look into. But I would
18 love to hear from others who have had experience with
19 them or from FDA and whether or not they have any
20 experience.

21 LAURA LEE JOHNSON: So, we are aware of
22 COMET. That may be part of the question. And I

1 think, also, there are a lot of other similar types of
2 initiatives. They're all different, but kind of
3 similar, as we were talking about, some of the COAs as
4 well.

5 And one of the elements here for our
6 focus was to make sure that that regulatory need was
7 going to be attended to. And so, I think we would
8 encourage folks to be looking at COMET and looking at
9 some of these other organizations that kind of try to
10 house what are these core outcome sets or other
11 elements like that, so it is an organic process.

12 But it's also important to note that,
13 you know, there are a lot of different ways to get
14 after core outcome sets. But, also, one thing we're
15 very interested in is the endpoint and making sure
16 that for us, for our sister agencies that many times
17 have different takes but are looking at those exact
18 same clinical trials that are being run, just from a
19 different perspective, and also the international
20 regulators. So, I think a lot of these groups that
21 have been involved with COMET have actually thought
22 about this, but there is some variety.

1 ROBYN BENT: Okay, Meena, do we have
2 another question?

3 MEENA SAVANI: Another question from
4 online: How will FDA ensure that core COAs developed
5 via this program are consistent with draft guidances
6 and that review divisions are engaged such that the
7 deliverables can support product development?

8 LAURA LEE JOHNSON: So, as our grantees
9 can attest, they've been assigned officers. So,
10 clinical said yes. After the review cycles were done,
11 clinical had to agree, like we're still invested,
12 we're putting forward our time and money. And, you
13 know, a lot of the groups that are involved, like
14 we're really short staffed, but we've all committed to
15 saying that we think this is important enough, as a
16 stakeholder, for the hours that our staff have to put
17 in looking at the 30 different COAs coming in on
18 different investigational new drug programs, can we
19 lower that down, can we gain some efficiency, that
20 we've made that commitment.

21 So, each of these programs has clinical
22 staff involved, statistical staff involved, clinical

1 outcome assessment staff involved. We're pulling in a
2 lot of different people, and so that is part of that
3 mandate that we have to also make sure that, yes,
4 we're interested. Everybody should know for your area
5 what those guidances are; we're looking at that, so
6 that level of what we also have for expectations as
7 we're thinking about tools -- again, FDA has put a lot
8 of not only our person power, but also our money, into
9 this. And part of that is to make sure that we, at
10 the end, to the best of our ability -- I mean, we're
11 not doing the exact work, but to the best of our
12 ability, that we can inform and make sure that we're
13 seeing the type of evidence that we need in order to
14 be able to use these tools longer term.

15 And we also have our sister centers
16 that we then also pull in, say hey, are we in
17 alignment? But most of our guidance is related to
18 patient-focused drug development, clinical outcome
19 assessments and the like. We do this as the three
20 centers, so we align. You know, good science is good
21 science, and so that's an important alignment that we
22 all have. We have slightly different regs, but we

1 work that out.

2 R.J. WIRTH: As one of the grantees, I
3 think that's one of the nicest parts about this
4 program is the interaction. And I was surprised by
5 just how much there is. Take that as you will.

6 But, no, seriously, we have monthly
7 calls, we have meetings. And as Laura Lee was saying,
8 it's not even just sitting on the phone with one
9 person. It's a group of people that are all very
10 interested in the project and how they turn out. So,
11 we have the statisticians; for our group, we have many
12 people from neurology; we have the COA staff online,
13 so there's really a constant dialogue.

14 What's great about that, not just are
15 we developing something that we can have confidence in
16 at the end of the day that will be acceptable, but
17 given the level of interaction and the frequency of
18 it, we're able to course correct very quickly. You
19 know, it's not waiting after two years, handing in a
20 dossier, then kind of going, okay, now I have to go
21 out and run another trial. You know, we can get on
22 the phone and say, we're thinking about doing this,

1 and have them go, well, you might want to think about
2 that more. Okay. And I think we're going to be able
3 to get a lot more done in a much more efficient
4 manner, given the level and frequency of
5 communications, because we can make sure we're heading
6 in the right direction in almost a continuous way.

7 ROBYN BENT: Thank you. Elektra, did
8 you want to add something?

9 ELEKTRA PAPADOPOULOS: No, I think the
10 areas that were initially put out with the RFA, with
11 the announcement, were areas that have unmet need, and
12 so we had buy-in even before going out with the
13 announcement. And so, there was a very strong
14 commitment to that.

15 ROBYN BENT: Okay, thank you. I think
16 we have one more question from the web.

17 MEENA SAVANI: We have one more
18 question, and I believe it builds off of a point
19 Elektra had made earlier in the panel discussion.
20 But, does the FDA expect that, once developed -- let's
21 say in about five years -- the core concepts will then
22 need to go through the DDT process for a specific

1 therapeutic area?

2 ELEKTRA PAPADOPOULOS: So, no, they do
3 not need to go through the DDT process because they
4 will be vetted, as was mentioned, throughout the
5 development of the core outcome set with the agency
6 using the multidisciplinary approach, using the good
7 measurement principles that the agency has
8 articulated. So, essentially, they will be -- our
9 expectation and our goal is that they will meet the
10 standards of fitness for purpose. It's just a
11 different program, and so they would not need to go
12 through that.

13 Now, they could. If they wanted, they
14 could achieve qualification, but we don't see the need
15 for that right now.

16 ROBYN BENT: Great, thank you. Do we
17 have any questions in the room? It looks like we do.

18 WOMAN 2: I want to thank everyone for
19 the commitment to patient involvement in this and the
20 idea behind it. I saw a lot of great expertise listed
21 on the slides who are part of the three programs being
22 done.

1 One thing I don't think I heard as much
2 about is expertise specifically in core outcome set
3 development. I know some of the names on there do
4 have it, but certainly COMET, ICHOM, some of these
5 other places, they all use a slightly different
6 methodology. I think I was reading an article
7 yesterday in a review of common articles where just
8 the definition of an endpoint in all of their review
9 ranged across disease areas from 12 to 5,776 different
10 endpoints that were used in these different disease
11 areas.

12 So, a lot of researcher discretion on
13 the definition of what makes an endpoint. Do you
14 include the timing of it? Do you include -- and the
15 idea of the concepts, whether or not you would have
16 multiple assessments that would be considered in
17 what's approved as opposed to one that's being
18 recommended, those sorts of things are all highly
19 dependent on the makeup of your committees and groups.
20 Is there people who have that expertise and have been
21 developing core outcome sets for many, many years to
22 have those lessons learned from what they've done as

1 they've gone through other disease areas that are
2 going to be part of the advising committees?

3 R.J. WIRTH: Well, this time, I won't
4 speak for the other programs. I don't think we have
5 anyone on our advisory committee or internally that
6 has had a sort of career looking at core outcome sets.
7 We do have a lot of experience in developing endpoint,
8 endpoint models and developing assessments, for us,
9 both within pharmaceutical and device, as well as in a
10 lot of other areas. So, I think there's extensive
11 experience and knowledge and know-how when it comes to
12 thinking about endpoints, and then the conversations
13 with the FDA to make sure that they're sort of in line
14 with their expectations. And there's a lot of
15 experience in developing assessment tools that we can
16 have confidence map onto those endpoints.

17 But, for our group specifically, there
18 is not somebody who has sort of had that career path.
19 But, again, I don't know about the other ones.

20 DEVIN PEIPERT: No, this is Devin from
21 NUCORE. Similar kind of statement, and I would echo
22 something that Laura Lee said earlier where I think

1 the focus is on, what are the needs of trialists and
2 people conducting trials and industry as they develop
3 new products, in terms of the outcomes, whether that's
4 an individual measure and a set of measures and
5 combinations. I mean, I think some of that stuff
6 comes through, in our experience, in different ways.
7 But I think the focus is on growing out of that field
8 and knowing what those experiences are from different
9 perspectives, more so than maybe some of the career
10 core outcome set folks.

11 WOMAN 3: So, I guess I'll third what
12 Devin and R.J. are saying. I mean, I think that we
13 would all be open to others' opinions, and we want to
14 make sure that we're kind of covering the gamut of
15 what's available. So, you know, we are certainly
16 willing to listen and be collaborative in this space.

17 KATIE GOLDEN: I just wanted to add
18 that, because there are three different groups and I
19 think that the dialogue has already started, you need
20 to use each other, because you all have different
21 learnings. So, you know, just consult each other.
22 You're all right here, so, yeah.

1 LAURA LEE JOHNSON: And so, I also want
2 to point out that there is a lot of methodology.
3 There are these different groups, as you mentioned,
4 and others as well. Some groups end up focusing more
5 on, when they say a core outcome set, they really
6 start talking more about concepts. And one thing that
7 has been a struggle for us at FDA and for other
8 regulators is -- and it's something that, in fact, one
9 of the reasons we have the qualification program was
10 to say -- because, we need the exact tool, and so it's
11 important to have the right concepts, so you've got to
12 start there. But then, how exactly is it being
13 measured? Because what may seem to be a small change
14 can actually have major ramifications about how this
15 is going to work in a trial.

16 And it's also, when we're trying to
17 think about how do we gain even more efficiency, is
18 thinking about, okay, how should it or should it not
19 be used in a trial, and what's the endpoint? So, part
20 of our discussion at the Guidance for Public Workshop
21 for our patient-focused drug development -- that's
22 tomorrow, if you want to spend another day watching

1 White Oak Live. But there also are certain elements
2 that become restricted when you work for the federal
3 government, and one is, for FDA and NIH, we actually
4 have something called the BEST glossary. And so, it's
5 Biomarkers, Endpoints, and other Tools. So, that is
6 where the two organizations -- we're required by
7 Congress, if I remember right -- to get together and
8 have, like, this is the definition that you're going
9 to use for certain things.

10 And so, while it is a living document
11 and it's on the National Library of Medicine's
12 website, there are certain parts -- and also, we have
13 ICH. We have other guidelines and guidances that we
14 do have to follow. And so, that is something that we
15 are also taking into account as we're looking at and
16 guiding these programs. But that's not to say -- and
17 I think we've consulted with groups that in fact have
18 that science of the core outcomes set, and not just --
19 so it's the S and not the A that we're looking at, and
20 that's something that we will keep in mind.

21 But if people have thoughts, if you all
22 have recommendations, as was mentioned at the

1 beginning, there is a docket to this meeting. But to
2 say, you know, based on what we heard, we think these
3 principles maybe aren't being adhered to. Can you
4 please look at this? Here's who to contact, things
5 like that. And so, you know, the substantive feedback
6 we can get through the docket, and this is the other
7 reason that we're having these meetings a couple of
8 times a year is to say, hey, here's transparency of
9 what's going on, where we are. Give us feedback. And
10 that's not me here at FDA, but everybody here and all
11 of their organizations to say, okay, what's the
12 feedback you have for us?

13 Again, maybe there will be a little bit
14 more course correction that happens if that's what's
15 necessary, or for folks to say, hey, this is how you
16 navigate these groups. It's an important feedback
17 mechanism that we have and we encourage you all to
18 use.

19 ROBYN BENT: Okay, I thank you all, and
20 I want to take this opportunity -- we are kind of out
21 of time for the panel conversation at this point, but
22 I think it was a really informative panel. And at

1 this point, we're just going to move on to our closing
2 remarks, because it has been an exceptional -- oops, I
3 should have looked at all the slides we had.

4 So, we're going to move on to the
5 closing remarks. It really has been an exceptional
6 day and a wonderful way for us to kick off our COA
7 grant program, by having this open public discussion.
8 And I'd like to so much thank everybody for staying
9 until the end. It's been very, very much appreciated,
10 and I really would just like to say thank you to
11 everyone who participated in person and on the web,
12 and who have come from long distances; all of our
13 panelists, our grantees, many of whom reworked their
14 scheduled in order to be here today. We very much
15 appreciate it.

16 For all of the feedback that we've
17 received, it will be taken back, discussed, and very
18 seriously considered. I also wanted to thank
19 everybody here at the FDA involved in both the
20 planning of this meeting and those participating in
21 the grant program, not only the staff of the patient-
22 focused drug development team who have worked

1 enormously long hours to prepare for this meeting, but
2 also the clinical review divisions, the Clinical
3 Outcome Assessment staff, and the Office of
4 Biostatistics staff, CDRH and CBER, all of whom have
5 committed to this effort on top of an already heavy
6 workload. And I really think it speaks to how
7 important we at FDA feel this effort is.

8 I want to share that our leadership, at
9 the highest levels, has been extremely supportive of
10 these efforts, and I want to quote Dr. Woodcock, our
11 center director, saying that patients really are the
12 true experts in their disease. And our hope is that,
13 with the development of these core outcome sets, we
14 can harness this expertise and incorporate it more
15 sustainable into the drug development process.

16 I can highlight some of the key themes
17 from the meeting, but I think it's really been done
18 well up until now. So, we heard about all of the
19 grant programs. We heard about the importance of
20 incorporating diverse patient populations. We've
21 heard and discussed a desire a little bit to include
22 more digital health technologies, but we also need to

1 consider the impacts of those on the patients who will
2 be using them. We heard from Katie about the burden
3 that patients struggle with on a daily basis and the
4 impacts that multiple things, including insurance,
5 have on her treatment choices.

6 We heard that what we've been doing
7 isn't always what we should be doing, but that we
8 really need to think about why we're doing things.
9 Some things we're doing great; some things we can
10 improve. We've heard about all of the exciting
11 projects related to COAs across the FDA and the
12 importance of stakeholder involvement, and the
13 importance of fitness for purpose and measurement
14 excellence. And we've heard about how the core sets
15 will continue to evolve as disease knowledge and
16 measurement science changes.

17 So, again, just a resounding thanks to
18 everyone who participated, and I would like to take
19 this opportunity to remind you that, if you were
20 unable to ask a question or if you have feedback that
21 you'd like to share with us, the public docket will be
22 open until January 6th. Please submit your comments.

1 We hope to see you tomorrow at the guidance
2 (indiscernible) workshop, and thank you very much.
3 Please, safe travels home.

4 (Whereupon, at 11:49 a.m. the
5 proceeding was concluded.)

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1 CERTIFICATE OF NOTARY PUBLIC

2 I, MICHAEL FARKAS, the officer before whom
3 the foregoing proceedings were taken, do hereby
4 certify that any witness(es) in the foregoing
5 proceedings, prior to testifying, were duly sworn;
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7 thereafter reduced to typewriting by a qualified
8 transcriptionist; that said digital audio recording of
9 said proceedings are a true and accurate record to the
10 best of my knowledge, skills, and ability; that I am
11 neither counsel for, related to, nor employed by any
12 of the parties to the action in which this was taken;
13 and, further, that I am not a relative or employee of
14 any counsel or attorney employed by the parties
15 hereto, nor financially or otherwise interested in the
16 outcome of this action.



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MICHAEL FARKAS

Notary Public in and for the

STATE OF MARYLAND

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I, SONYA LEDANSKI HYDE, do hereby certify that this transcript was prepared from the digital audio recording of the foregoing proceeding, that said transcript is a true and accurate record of the proceedings to the best of my knowledge, skills, and ability; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this was taken; and, further, that I am not a relative or employee of any counsel or attorney employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

SONYA LEDANSKI HYDE

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