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2 U.S. FOOD AND DRUG ADMINISTRATION
3 CENTER FOR DRUG EVALUATION AND RESEARCH
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6 PUBLIC WORKSHOP ON
7 PATIENT-FOCUSED DRUG DEVELOPMENT:
8 GUIDANCE 1
9 COLLECTING COMPREHENSIVE AND REPRESENTATIVE INPUT
10

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12 FDA White Oak Campus
13 10903 New Hampshire Avenue
14 Building 31, Room 1503 (Great Room)
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17 Monday, December 18, 2017
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1 P R O C E E D I N G S

2 WELCOME

3 MS. VAIDYA: We'll go ahead and get started
4 now. I know there are still some folks trying to
5 get through security. Okay. Good morning,
6 everyone. My name is Pujita Vaidya, from the
7 Office of Strategic Programs in the Center for
8 Drug Evaluation and Research, also called CDER.

9 I'd like to welcome everyone to our public
10 meeting today, the first in a series of meetings
11 that we'll be conducting as CDER and CBER work
12 together to develop several patient-focused drug
13 development guidances throughout the year.

14 We are happy to see so many patients, patient
15 advocates, academic researchers, expert
16 practitioners, drug developers and other very
17 important stakeholders in the audience today. And
18 I also understand that we have many more joining
19 us remotely from the Web. So thank you all for
20 being part of this meeting.

21 In our discussion today, we will be focusing
22 on topics related to our Guidance 1 document,

1 approaches to collecting comprehensive and
2 representative input and patient and caregiver
3 input on burden of disease and current therapy.

4 Throughout the day, we want to hear from you
5 and get your comments and feedback on the
6 approaches and considerations that are proposed in
7 our discussion document that we put out about a
8 month ago. If you have not gotten a chance to
9 read through the document, that is okay. We will
10 be going over the key points in our presentations
11 and discussions throughout the day today.

12 I do want to mention that in addition to this
13 meeting, a docket will remain open until February
14 16, 2018 to which the public may submit general or
15 detailed comments regarding the specific aspects
16 of the discussion documents or other topics raised
17 throughout the meeting.

18 We do have a full agenda for today and for us
19 to keep our conversation flowing and our
20 discussion moving, our moderators may need to jump
21 in and ask you to provide a little bit -- provide
22 detailed comments to our docket or discuss with --

1 or you may have the opportunity to discuss with
2 your colleagues during the breaks.

3 Now, let me quickly go over the agenda for
4 today and walk through that. So first, we'll
5 start off with Theresa Mullin, director of CDER's
6 Office of Strategic Programs, who will get us
7 started with the morning -- in the morning with
8 her opening remarks.

9 We will then have two presentations, first
10 focused on FDA's approach to defining key
11 terminology and developing the glossary, and then
12 the second on FDA's approach to developing FDA's
13 Guidance 1 discussion document.

14 We will then have panels focused on
15 considerations on specific topics. The panel
16 sessions will be as follows: session one, defining
17 research objectives and methodological
18 considerations for designing studies to collect
19 patient experience data.

20 Session two will be on methodological
21 considerations for data collection, analysis and
22 operationalization. Session three, translating

1 best practices into real practice, developing
2 guiding examples. And finally, session four on
3 identifying key themes and next steps.

4 Throughout the day, the audience will have
5 several opportunities to ask questions and provide
6 their views. We have many people attending via
7 the Web. However, we will not be able to take
8 comments or questions from the Web during the
9 meeting. So we encourage you to please submit
10 your comments to the public docket.

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

15 Participation is on a first-come, first-serve
16 basis. We have 30 minutes allocated for this, for
17 this time, and we can take up to 15 speakers,
18 although we do hope that you get an opportunity to
19 ask questions throughout the day since we have
20 built in several Q&A sessions.

21 Before I get started with some brief
22 housekeeping items, I would like to ask my FDA

1 colleagues sitting here on my left to introduce
2 themselves. This panel will be in active
3 listening mode throughout the day. And then, for
4 each session that I just walked through, we will
5 have a separate panel of speakers joining us up
6 front here as well. With that, I'll turn it to
7 Theresa.

8 DR. MULLIN: Good morning. It's Theresa
9 Mullin. I direct the Office of Strategic Programs
10 in the FDA Center for Drugs.

11 DR. JOHNSON: I'm Laura Lee Johnson. I'm the
12 acting director, Division of Biometrics III in
13 CDER and I'm also the patient-focused drug
14 development liaison for the Office of
15 Biostatistics.

16 DR. PAPADOPOULOS: Good morning. I'm Elektra
17 Papadopoulos. I am the associate director for
18 clinical outcome assessment staff here in CDER.

19 DR. IRONY: Good morning. I'm Telba Irony.
20 I'm in the Center for Biologics and in the Office
21 of Biostatistics and Epidemiology.

22 DR. LEE: Good morning. I'm Kerry Jo Lee.

1 I'm a medical officer on the guidance and policy
2 team within the Office of New Drugs, CDER.

3 DR. KOMO: Good morning. My name is Scott
4 Komo. I am a statistician in the Office of
5 Biostatistics at CDER.

6 DR. DANIELS: Good morning. My name is Selena
7 Daniels. I'm a team leader on the clinical
8 outcome assessment staff in CDER.

9 MS. VAIDYA: Thank you. So just a few brief
10 housekeeping items, this meeting is being
11 transcribed and a live webcast is being recorded,
12 both of which will be archived on our website.

13 We will have an hour lunch break at around
14 11:30 after session one and then a 15-minute break
15 in the afternoon at 2:45 after session three.
16 However, please feel free to step out to stand up
17 and stretch as needed throughout the day.

18 There are food and beverages available to
19 purchase at the kiosk outside of the room in the
20 lobby. We strongly encourage you to preorder your
21 lunches. So if you have not done so already, we
22 definitely encourage you to do that.

1 Bathrooms are down the hallway in the lobby to
2 the left, to the right. And then, Wi-Fi password
3 is available at the registration desk and we did
4 have it up earlier. So with that, I would like to
5 now invite Theresa Mullin to the podium for
6 opening remarks.

7 OPENING REMARKS

8 DR. MULLIN: Thank you, Pujita. Good morning,
9 everyone. And I just want to begin by saying we
10 are very happy to have you here today in the room
11 and on the webcast. This is a very exciting
12 meeting for us. It really marks a milestone in
13 like the second phase of the patient-focused drug
14 development effort that we have been undertaking
15 here.

16 And, just to give you a little bit of
17 background on this, about five years ago, a little
18 over five years ago, we had our first meeting to
19 talk about which diseases we should really be
20 focusing on in what we consider to be a sort of
21 pilot effort to see what could we do to better
22 hear directly from patients about what it felt

1 like to live with their disease and what they were
2 doing to treat their disease.

3 We received a lot of comments. We took sort
4 of an experimental approach. We didn't really
5 know how to approach this. But we had over 24
6 meetings that we conducted in this room and we've
7 learned a huge amount, very powerful information
8 that we learned from patients about each of their
9 diseases.

10 But we also came away with some broader
11 learnings than that. And this included that our
12 coming to really understand and recognize that
13 patients are experts, that they have -- that they
14 are key informants to the development of drugs and
15 to their care and that we needed to consider them
16 as such and more systematically incorporate their
17 perspective, their knowledge into drug development
18 and our decision-making.

19 We often found that in our listening to them
20 talk about their disease and their treatments,
21 that their chief complaints were not necessarily
22 factored into the development plans or captured

1 very well in the measures of benefit that would be
2 collected during those trials.

3 So we concluded, we realized and we heard from
4 our stakeholders, who were also trying to help us
5 figure out where do we go next with this, the
6 meetings -- those patient-focused meetings are a
7 critical part of this effort. And we hope that
8 the continue and we plan to continue to engage in
9 those kinds of meetings as we identify the need to
10 do so.

11 And there's an externally led approach that
12 many of you are aware of that we also are working
13 with stakeholders to take advantage of.

14 But we realized that we needed to engage you
15 all in trying to figure out the best, best
16 methods, the "fit for purpose" approaches to
17 bridge from those early qualitative meetings to
18 collect meaningful, measurable input that can be
19 used in trials and be used as part of our
20 decision-making when it comes to drugs and then
21 issue guidance based on that.

22 And so, in the PDUFA reauthorization -- that's

1 the Prescription Drug User Fee Act, which funds
2 most of our work on new drug review at the FDA --
3 we committed to develop four guidance documents,
4 and there's a relationship between these four.
5 And you'll hear, certainly if you've read the
6 document, the guidance -- the discussion draft
7 that Pujita mentioned, you know a bit about this
8 already.

9 But there's definitely a dependence and a
10 relationship and the first one is the one we're
11 going to be talking about today. That's the
12 collecting comprehensive patient community input
13 on burden of disease and current therapy.

14 And then, following that, one on developing a
15 holistic set of impacts, including disease burden
16 and treatment burden that are most important to
17 patients, identifying good measures that can be
18 included that actually would help reflect the
19 effectiveness of a therapy being studied in a
20 trial and, finally, what measures to include that
21 could be considered in regulatory decision-making.

22 And for each of these, we committed, as part

1 of this agreement under the Prescription Drug User
2 Fee reauthorization, which was enacted in August
3 of this year, to have a workshop first, to hear
4 from stakeholders, make sure we were capturing
5 everything that they thought of, the methods that
6 they were using, the experiences that they've had.
7 So we got the benefit of that as we moved toward
8 developing a draft guidance.

9 And these guidances in the Prescription Drug
10 User Fee Act are very well-aligned with the
11 requirements for guidance that were put in place
12 by Congress a little bit over a year ago, mid-
13 December of last year, the 21st Century Cures Act
14 was enacted.

15 And Title III, Subtitle A speaks to patient-
16 focused drug development. And in particular,
17 section 3002 outlines eight provisions, the first
18 four of which are very well-aligned with the
19 commitments that we have in the PDUFA again, which
20 is great for us.

21 So you see again highlighted in orange lots
22 more words, but we're going to talk about that

1 same intention that we have. And you'll be
2 hearing about it all day.

3 But we'll be covering these four -- first four
4 components of 3002 in our four guidances. And
5 actually, we're going to cover some of these
6 others as well, although I'll point out right now
7 and say number five here, in the 21st Century
8 Cures Act, of this provision is about FDA issuing
9 guidance to stakeholders who want to submit
10 guidance to us and how to do that in the most
11 effective way and the most successful way.

12 And we'll be having a public meeting about
13 that in March of next year. And some of these
14 others, we'll be addressing all of these. We have
15 a plan on our website that tells you exactly how
16 we're going to go about it.

17 But this work is very exciting and it marks a
18 new phase of our work. And along those lines,
19 here is a picture that says -- just tries to
20 convey that we really see that there are
21 opportunities to collect patient experience data
22 throughout the drug lifecycle.

1 And here, you see what you might consider to
2 be stages in the drug lifecycle, from discovery,
3 preclinical development into clinical trials
4 development. FDA reviews a dossier based on that
5 development program and then, following that,
6 post-market safety. And so, we really see
7 opportunities in every step.

8 And here are just some illustrative activities
9 to convey that. In the discovery phase, or very
10 early on, you might be engaging in identifying
11 what the disease impact and treatment burdens are
12 that patients and their families are most
13 concerned about and really try to figure out how
14 to address those in your development programs.

15 And in the next phase, further after doing
16 that initial work, you may be completing
17 identifying and developing and testing those data
18 collection instruments to ensure that they're
19 ready for use in trials.

20 But you could also be doing that earlier on in
21 the development phase. So that's why that little
22 orange box is there. I came up with this color

1 scheme, my very crude PowerPoint skills. But
2 that's to convey you can be doing that even
3 earlier.

4 But then, when you get to trials, you're
5 conducting the trials and trying to assess whether
6 the changes in those clinical outcome assessments
7 during the studies are meaningful and are they
8 clinically meaningful to the patient.

9 And finally, you're going to possibly be
10 collecting information post-market to really
11 understand the degree to which those benefits and
12 risks that you reported on during the clinical
13 development phase are consistent with what's
14 happening in the larger population post-approval.

15 And what you see below here is our attempt to
16 convey that we think the four guidances that we've
17 committed to do and we'll be talking about over
18 the next four years are really going to help
19 inform and support all of those stages of patient
20 experience data collection.

21 And finally here, the questions that we have
22 for you today, and you'll know these questions

1 already. They're in the Federal Register notice
2 that we put out for this meeting. But we'll be
3 asking and listening for what is the level of
4 detail that you think is appropriate for these
5 guidance documents.

6 We want to try to hit that sweet spot of
7 enough but not overwhelming people with too much
8 information. And what is the document structure
9 and content that would be most useful in these
10 guidances? We want them to be very usable for
11 you.

12 Does the document make clear that we
13 understand that the research methods that we talk
14 about in the guidance document are some of the
15 ones which you may be using. But we're open to
16 hear about other methods as well and that may
17 occur in a proprietary drug development program or
18 in the precompetitive space and be more publicly
19 available.

20 What are the most important time points when
21 we all have to say come talk to FDA? I mean, we
22 have limited resources. But we want to pick those

1 times which, in your experience or with your work,
2 you think would be most valuable to get FDA's
3 input.

4 And then, finally, we're going to present to
5 you -- Meghana is going to, in a moment, present
6 to you that glossary of standardized terms that
7 we've put together.

8 And are these proposed draft definitions that
9 we've come up with clear and do they facilitate
10 the dialogue and the discussion and do they really
11 support the development work. And so, those are
12 our questions for you and we very much look
13 forward to hearing from you today.

14 And with that, I'll turn it over to Meghana
15 Chalasani.

16 PATIENT-FOCUSED DRUG DEVELOPMENT: DEFINING KEY

17 TERMINOLOGY

18 MS. CHALASANI: Thank you, Theresa, and thank
19 you all. It's so great to see so many people here
20 bright and early Monday morning in the Great Room.
21 Okay. So, hello. My name is Meghana Chalasani
22 and I'm in the FDA's Center for Drug's Office of

1 Strategic Programs.

2 As Theresa mentioned in her opening remarks,
3 PDUFA-VI commitment for a glossary that's relevant
4 to all four guidance documents. And so -- oops,
5 if I can move these slides. There, great. Thank
6 you, Theresa. Thank you.

7 Okay. So the goal of this glossary is to
8 provide standardized nomenclature and
9 terminologies related to patient-focused medical
10 product development.

11 And a few key considerations regarding the
12 scope of this glossary and to keep in mind as you
13 read and use are that the terms are relevant to
14 all four of the methodological PFDD guidances that
15 Theresa mentioned.

16 There may be terms that are defined in the
17 glossary that you may not see in a discussion
18 document for this workshop or in the first
19 guidance either. But it may be relevant to a
20 topic in one of the following future guidances.

21 We did not want to reinvent the wheel when we
22 were developing this glossary, nor did we intend

1 it to be completely exhaustive either. The terms
2 in the glossary are defined specifically for the
3 context of medical product development, evaluation
4 and regulatory decision-making.

5 Sorry, I'm having a difficult time with these
6 slides. They're just not cooperating. I think
7 they just really liked my pretty background and
8 they're just trying to keep it up there. All
9 right. Let me try to click on it. I think this
10 might be better to keep.

11 Okay. Great. So on this slide, you'll find a
12 high level overview of how the glossary was
13 developed. So identify terms, FDA conducted a
14 literature review and outlined the topics that
15 will be addressed in the PFDD guidance series.

16 As I mentioned, we really did not want to
17 reinvent the wheel. And so, we curated any
18 existing definition using federal resources,
19 literature and other external resources as well.

20 And the development process was truly
21 collaborative across our medical product centers.
22 We had cross-center facilitated discussions with

1 experts from our Center for Drugs, Biologics and
2 Devices to determine the relevant terms and their
3 definitions. There were also multiple
4 opportunities to seek feedback from other FDA
5 colleagues.

6 And just to kind of provide a high level
7 overview and bring it all together, in the
8 glossary, we defined patient-focused drug
9 development, also referred to as patient-focused
10 medical product development.

11 We also defined the who. So, who do we
12 collect information from? Patients, caregivers,
13 patient representatives. The how, so the how do
14 we collect? Patient engagement and the preference
15 methods and so forth. And the how well, fit for
16 purpose, methodologically sound. And we also did
17 the what.

18 And this glossary is really intended to be a
19 living document. FDA plans to post the glossary
20 on its website so that it can be updated
21 periodically. This version that FDA has posted
22 for the workshop is really just a draft.

1 And so, we really are asking all of you to
2 provide us feedback through the docket. You'll
3 find the link here and these slides will be posted
4 on our workshop website afterwards. And the link
5 is also at the end of your agendas.

6 And so, the docket will be open until February
7 16th, as Pujita and Theresa mentioned. So please
8 provide us with your feedback. Please keep the
9 scope of the glossary in mind, remembering that
10 it's supposed to cover all four of the
11 methodological guidances.

12 And let us know if there are any terms that we
13 may have missed or if there are any definitions
14 that are not clear or not understandable. And
15 that's really just a quick overview of the
16 glossary. Thank you.

17 MS. VAIDYA: Thank you, Meghana. I'd like to
18 now invite Laura Lee Johnson, from CDER's Office
19 of Biostatistics to provide an overview of FDA's
20 approach to developing the PFDD Guidance 1
21 document.

22 OVERVIEW OF FDA'S APPROACH TO PFDD GUIDANCE 1

1 DR. JOHNSON: Good morning, everybody, and
2 welcome on behalf of CDER's Office of
3 Biostatistics and Office of Translational Sciences
4 and also on behalf of my colleague, Elektra
5 Papadopoulos, who's head of the COA staff in the
6 Office of New Drugs.

7 So we're going to catch up some of the time
8 here today and talk about our ultimate purpose.
9 So right now, our goal is to understand those
10 patient perspectives on benefits and risks.

11 So starting off with the definition, we have a
12 clinical benefit which is the positive clinically
13 meaningful effect of an intervention, so the
14 positive effect of how an individual feels,
15 functions and survives.

16 Now, traditionally, people have thought about
17 how long a patient lives. So they think about
18 survival. But we also care quite a bit about how
19 a patient feels or functions in daily life. And
20 that may mean an improvement in how they feel or
21 function, but it also may mean prevention or
22 slowing of anticipated decline.

1 A clinical outcome is defined as the outcome
2 that describes or reflects how that individual
3 feels, functions or survives. And we tend to
4 assess these using clinical outcome assessments,
5 and you'll hear us say COA or C-O-A for short.
6 But we'll try to use all of the words today.

7 But what we really want to focus on is that
8 careful assessment of patients' views on benefits
9 and risks and how they're important to part of our
10 regulatory decision-making.

11 So what is patient experience data? As
12 Theresa pointed out, we have a definition in the
13 21st Century Cures Act and we're looking at data
14 that is collected about any persons and are
15 intended to provide information about patients'
16 experiences with a disease or condition.

17 That includes experiences, perspectives, needs
18 and priorities of patients related to, but not
19 limited to, symptoms of their condition and its
20 natural history, so understanding what patients
21 are experiencing there, the impact of the
22 conditions on their functioning and quality of

1 life, experience with treatments, input on which
2 outcomes are important to them, patient
3 preferences for outcomes and treatments and the
4 relative importance of any issue as defined by
5 patients.

6 So why is it important to collect the patient
7 experience data? As Theresa mentioned, patients
8 are experts in their own experience of their
9 disease. Many of us have described this. They're
10 experts in their experience of the disease or
11 condition and they're also the ultimate consumers
12 of medical products.

13 Patient experience data can inform medical
14 product development. It also enhances our
15 regulatory decision-making to address a patient's
16 needs.

17 So where does the data come from? It's the
18 patient's journey and it should be defined by the
19 patient's perspective, where possibly. It's also
20 informed by input from patient partners and
21 clinicians. We may need to have a multipronged
22 approach in order to reach and cover our target

1 populations.

2 So we have several different types of patient
3 partners. Many of us think about the patient.
4 But we also have caregivers or care partners who
5 help patients with daily activities, their
6 healthcare, other activities a patient may not be
7 able to perform due to illness or disability.

8 This person may or may not have decision-
9 making authority for the patient and is not the
10 healthcare provider. Patient advocacy groups are
11 also part of our patient partners. And this may
12 be a group of individuals.

13 They may or may not be part of that target
14 population. But these are people who have a role
15 in promoting an interest or cause to influence
16 policy with respect to patients' health or
17 healthcare.

18 Now again, as Meghana mentioned, we have a
19 glossary. And so, if you want changes to some of
20 these definitions, this is the type of information
21 to submit to the docket.

22 Now, when do you collect patient experience

1 data? This is a key element. Input should start
2 early and it might be before or throughout that
3 medical product development process.

4 Precompetitive collaboration is encouraged. You
5 may have heard about our qualification program for
6 clinical outcome assessments. But an important
7 element is this information may come through an
8 individual drug or medical product program.

9 It might come from outside in a precompetitive
10 space and many times this precompetitive work can
11 actually help move an entire disease area's
12 research and development forward. So what we're
13 talking about today can be used in a lot of
14 different areas.

15 Who can collect and submit patient experience
16 data? Anyone can collect and submit that data.
17 That includes patients, family members or
18 caregivers of patients, patient advocacy
19 organizations, disease research foundations,
20 researchers and drug manufacturers. And today, we
21 in CDER and throughout FDA get information from
22 all of these different groups.

1 How can external stakeholders submit that
2 experience data to FDA? Stay tuned, but a lot of
3 various pathways exist. We have under development
4 FDA guidance on how to submit information in order
5 to broaden and clarify how this information can
6 come in.

7 But what's also important is to understand
8 that, depending on the purpose and type of data,
9 different content and formats may be appropriate.
10 And so, we are refining this and making sure that
11 we're going to be able to have the most efficient
12 path for everybody in the office and for those of
13 us at FDA.

14 How is patient experience data used for
15 regulatory purposes? We use it to inform clinical
16 trial design, as do many of the manufacturers and
17 sponsors and companies that we work with. It
18 might be that this type of information helps us
19 consider what the appropriate control group should
20 be.

21 It can help us consider a lot of different
22 logistics for the trial. Also, may say, okay,

1 what is the natural history, what should we be
2 considering.

3 But this leads also into that trial endpoint
4 development and selection. In particular, if
5 there's debate about what a primary endpoint
6 should be, what is it that patients are really
7 looking for.

8 But then also thinking about our reviews
9 including benefit and risk assessment, how much
10 change do patients want and how much risk and in
11 what areas are they willing to take.

12 So how do we collect this information? We
13 recommend qualitative, quantitative or mixed
14 methods to collect robust and meaningful patient
15 experience data. Selena Daniels will be talking
16 more about these different types of methods in the
17 afternoon. And they are described in the
18 discussion document.

19 But the main element to consider is that
20 really we need fit for purpose methods to get to
21 the goal. So consider what your goal is. Again,
22 this multipronged approach. Rarely will a single

1 study answer all questions. That's true for
2 anything in clinical research.

3 But Guidance 2 is going to talk more about
4 this because sometimes there are very specific
5 elements to consider. What is the question? What
6 is the approach? And what is the answer that we
7 are seeking?

8 Now, we mentioned a little bit about those
9 four guidances and I'm going to step us through
10 these because our meeting today and the docket
11 that's open is for Guidance 1, collecting the
12 comprehensive patient community input on burden of
13 disease and current therapy.

14 So you can think about this as what people am
15 I gathering together to get information from. Who
16 do you ask? How do you get that input from them
17 and why are you choosing this group of people?
18 How do you collect the information?

19 So things like you're going to have a lot of
20 examples in the afternoon -- who do I gather.
21 This is the underpinning for all of the other
22 guidances in all types of work. It's an important

1 question from your very early questions, all the
2 way to your final research qualitative work that
3 may happen.

4 Our second guidance gets into development of
5 that holistic set of impacts. So a little bit of
6 how do you collect it and part of what Selena is
7 talking about today in the afternoon will actually
8 flow into the second guidance. So if you provide
9 input on that, it may be something that we
10 consider for the guidance that we're working on
11 for next year.

12 What do you ask? Guidance 1 gets together the
13 group. Guidance 2, what do I ask them? Why am I
14 asking them these particular questions? How do I
15 ask a non-leading question that's well-understood
16 by a wide range of patients and others?

17 How do I avoid getting misleading results? A
18 lot of times, if you slightly tweak the question,
19 you may end up with a very different answer. So
20 we need to think about how we are actually getting
21 the information from that group that we've put
22 together under Guidance 1.

1 And Guidance 3, we're deciding what to measure
2 in a clinical trial. So in Guidance 2, I have a
3 long list of impacts that are important to
4 patients. Guidance 3, we're trying to hone down
5 that list. How will I select what to measure in
6 that clinical trial, refining that set of impacts
7 to what's actually measurable? It might be an
8 important concept.

9 Do I know yet how to actually measure it?
10 What's going to be most likely to show clinical
11 benefit in a specific treatment trial? Sometimes
12 we have elements that might be extremely important
13 to patients and their families. But we know that
14 the treatment is not going to impact that
15 particular issue. And so, that's not your best
16 primary endpoint direction to go.

17 But four gets down to the final part of what
18 should a primary endpoint, for example, be in a
19 trial, identifying and developing good measures
20 for those identified sets of impacts from Guidance
21 3 and incorporating clinical outcome assessments
22 into endpoints. So for example, my clinical

1 outcome assessment, I might ask people questions
2 every single day, something called a daily diary.
3 How do I summarize that information into an actual
4 endpoint in the trial?

5 But we also need measures and endpoints that
6 are considered significantly robust for regulatory
7 decision-making. So that's the information that
8 will be in Guidance 4. What is the right endpoint
9 and how do I select the tool to be in my trial?

10 But our purpose today is Guidance 1. We're
11 going to start from the beginning, as they say.
12 Who are the people that we're trying to put
13 together to get information from? We're going to
14 talk this morning about a set of methods for
15 collecting information on patient experience
16 that's representative of the intended population.

17 And our four lead authors, three of whom will
18 be presenting today and one of whom is taking a
19 lot of notes in the audience, we are going to hear
20 from them today with a brief synopsis of their
21 sections of the draft document, because I'm sure
22 everybody's read it intently. But just in case,

1 we'll have that.

2 So Selena and Ebony and Kunthel will give you
3 a brief overview of that discussion document today
4 because we also want to present a synopsis of
5 methods that will be further elaborated in our
6 later guidances on how to operationalize and
7 standardize data collection, analysis and
8 dissemination of the patient experience data.

9 A focus for us to consider is we're going to
10 try to not get too methodological in today's
11 discussion. If you have a deep methodological
12 area that you want to go into, please submit it to
13 the docket because our guidance is set up in a way
14 that's different than many FDA guidances.

15 We have a very broad audience to serve and we
16 also want to make sure that the people today both
17 in the room and online can participate and
18 everybody, regardless of your training, can have a
19 deep understanding of where we are going and what
20 we want to do.

21 So this is a focus for discussion among FDA
22 and multiple stakeholder groups, with our patient

1 partners really being first. This is intending to
2 encourage patient involvement as partners before
3 and throughout the medical product development
4 process and to promote a collaborative process in
5 the collection of robust patient experience data.

6 Guidance 1 emphasizes the concept of fit for
7 purpose, as will our other guidances. So the
8 tools match the specific research questions and
9 our regulatory needs. And we also want to make
10 sure that it's recognized that the science of
11 patient input is evolving field.

12 So this is something that you'll notice was
13 one of the specific questions asked up front and
14 in our closing remarks I'll be asking again.

15 We've heard many times from our sponsors that
16 the regulatory groups inside the companies will
17 point to FDA guidances and say what you want to do
18 is not specifically spelled out here. So you
19 can't do it. That's not what we want to have
20 happen.

21 It says in almost every FDA guidance, if you
22 want to do something else, come talk to us. We

1 mean it. So one of our large points here is this
2 is an evolving field. What's missing that we
3 should be putting into an ultimate guidance for
4 Guidance 1?

5 But then also, is it understood that, as
6 methods come up, we want you to come and talk to
7 FDA about what you want to do? And even for
8 methods that may not be listed, again, we want you
9 to come to FDA to talk to us about what you want
10 to do.

11 Our approach also recommends, we hope, a
12 pragmatic stepwise way to provide usable patient
13 experience information to FDA. So does Guidance 1
14 address clinical outcome assessments or patient
15 preference information? We've been asked this
16 question before we came up. So we decided,
17 Elektra and I, to address it directly.

18 Guidance 1 provides a framework for collecting
19 representative patient input that can be used to
20 inform clinical outcome assessments, patient
21 preference information and a whole host of other
22 types of research. It does not cover collecting

1 or analyzing clinical outcome assessment or PPI
2 data directly, that patient preference information
3 directly. Some of those issues are in other
4 guidances to industry out of FDA. So a couple of
5 those are listed. But again, this is a basic
6 framework for collecting representative patient
7 input.

8 So today, we're going to start off in the next
9 session where Ebony and Kunthel will talk about
10 general considerations for collecting patient
11 experience data, going through defining the
12 research questions and objectives, from whom to
13 collect information, looking at determining the
14 study design and research setting, constructing a
15 sampling frame and additional considerations to
16 achieve sufficient representation.

17 Then, in the afternoon, Ebony will talk about
18 the methods for collecting and analyzing data.
19 Again, this is the beginning. We're going to do
20 more in Guidance 2 and later guidances, and then
21 operationalizing and standardizing data collection
22 and data management. And with that, I'll turn

1 this back over.

2 MS. VAIDYA: Thank you, Laura Lee. Now, we'll
3 move into Session 1. This session will be
4 moderated by Michelle Campbell, from the clinical
5 outcome assessments staff in the Office of New
6 Drugs in CDER. And I'd also like our panelists to
7 please join us up here. With that, I'll turn it
8 over to Michelle.

9 SESSION I: DEFINING RESEARCH OBJECTIVES AND
10 METHODOLOGICAL CONSIDERATIONS FOR DESIGNING STUDIES TO
11 COLLECT PATIENT EXPERIENCE DATA

12 DR. CAMPBELL: Good morning. My name is
13 Michelle Campbell and I'm with the clinical
14 outcome assessments staff in the Office of New
15 Drugs in CDER. It's my pleasure to begin our
16 sessions today taking a closer look at the
17 discussion document we have drafted.

18 The first session we will discuss will look at
19 considerations when determining the study defines
20 and research setting, including selecting a
21 sampling frame when collecting patient experience
22 data.

1 With us for this session today, I have my
2 colleagues Ebony Dashiell-Aje, from the COA staff,
3 and Kunthel By, from the OB, along with Steve
4 Cohen, from RTI International, Richard Gershon,
5 from Northwestern University, Mia Karr, from the
6 National Center for Health Statistics and Liz
7 Piault-Louis, from Genentech.

8 Unfortunately, our patient advocacy
9 representative, Suzanne Vernon, from the Bateman
10 Horne Center, which is a patient advocacy group
11 for MECFS was unable to join us today. However,
12 Suzanne did send us some comments and thoughts and
13 I'll be sharing them later as we continue this
14 session.

15 How we're going to do the session today is
16 we'll be seeing a brief presentation from Ebony
17 and Kunthel. And they're going to be discussing a
18 little bit more looking at how we define our
19 research objectives and sampling frame.

20 We will then turn it over to our panelists to
21 give their initial thoughts and go into some
22 deeper discussion with the panelists and a couple

1 of questions. We will end with questions and
2 comments from our audience, if you have any.
3 Please know that if we do not get to your
4 questions or comments, please consider putting
5 them on the docket, which is a recurring theme
6 you'll be hearing all day today.

7 But we do encourage you to make sure that if
8 you don't feel that your voice was captured today
9 or you have additional thoughts, to please make
10 sure you go to the docket.

11 So I'm going to turn it over to Ebony, who
12 will start our presentation.

13 FDA PRESENTATION

14 DR. DASHIELL-AJE: Good morning, everyone. So
15 today, in this first session, Kunthel and I will
16 discuss potential methodological considerations
17 and practical implications for defining research
18 objectives and designing studies to collect
19 patient experience data.

20 So when determining the best approach for
21 conducting research to collect patient experience
22 data, there are a number of factors that should be

1 considered during the study and design phase.
2 These include research goals and questions to be
3 addressed, the target population under study,
4 which includes recruitment feasibility, as well as
5 factors related to the amount of time to collect
6 the data and study budget.

7 Now, if there are constraints related to time
8 and budget, you should consider scaling back
9 objectives and questions. Along with these, you
10 should also consider the type of information that
11 you generate from the study, including the value
12 of that information, short-term and long-term
13 impacts of the information that you intend to
14 generate as well.

15 And all of these factors, as outlined in this
16 diagram and in the discussion document, are
17 equally important to consider when selecting the
18 most appropriate research approach and to ensure
19 the success of a study.

20 So the following are some general steps that
21 we've outlined in the discussion document and
22 subsequent appendices to help provide guidance

1 during the study and design phase. As these steps
2 are outlined, decisions can be made to determine
3 what the most appropriate research approach will
4 be for a study.

5 Within the guidance and discussion document,
6 we intend to discuss these elements in detail and
7 my colleague, Kunthel, and I will give a brief
8 overview of steps one through five, while my
9 colleague, Selena Daniels, will pick up on steps
10 six through eight in session two today.

11 So how do you define research objectives and
12 questions? Research objectives should be specific
13 and defined by research questions. Subsequently,
14 these will inform the methodological decisions
15 that you make for your study. For instance,
16 whether you're going to use qualitative,
17 quantitative or a mixed methodology to generate
18 data and analysis plans.

19 When defining research questions and
20 objectives, you should consult the literature, as
21 well as content experts to determine what
22 information each question or objective will yield

1 and whether this information will best meet your
2 study goals.

3 So here's an example that we've presented in
4 the discussion document to help illustrate the
5 relationship between research objectives,
6 questions and study design considerations and
7 characteristics. So within this example, we've
8 provided a case study of HIV. We've given a
9 sample research objective, along with proposed
10 questions that can help define that research
11 objective, and the potential next steps for
12 designing a study and specifically a qualitative
13 study that can help address the potential research
14 questions of interest.

15 So once you determine the objectives and
16 questions that you would like to investigate, you
17 should then determine the most appropriate target
18 population to obtain this information from. And
19 we've provided this example, just like with the
20 research objectives and questions example, to help
21 researchers understand what constitutes a target
22 population in a given study.

1 For this example, we're taking from
2 Parkinson's disease and we're trying to define the
3 target population for you all. Now, when you are
4 defining the target population, it's important to
5 communicate with the agency to make sure that the
6 proposed target population is aligned with
7 regulatory needs.

8 So when determining from whom to collect this
9 information, it's important to consider who would
10 be the best reporter of the patient experience
11 information that you want to collect. So the
12 following are a number of factors, including, but
13 not limited to, age, level of cognitive
14 development, communication skills, health
15 literacy, the level of insight that a patient
16 might have on their condition, health state and
17 comorbidities.

18 Taking it a step further, here's a case
19 example that we've provided in the discussion
20 document regarding age to help illustrate factors
21 that should be considered when determining who
22 would be the most appropriate source of

1 information in a study designed to collect patient
2 experience data.

3 In this example, we outlined considerations
4 for determining the youngest age of self-report
5 and the most appropriate informant based on
6 developmental limitations.

7 Some other important points to consider are
8 related to subgroups. When possible, subgroups
9 should be pre-specified during the study design
10 phase.

11 Likewise, we should consider the number of
12 subgroups being processed -- proposed, excuse me -
13 - for analysis and inference; the reporter type,
14 including patients versus primary caregivers;
15 reporter characteristics, socioeconomic,
16 demographic, cultural, linguistic, et cetera; and,
17 prevalent symptoms for disease or conditions with
18 notable symptom heterogeneity.

19 So I will now turn the rest of this
20 presentation over to my colleague, Kunthel By, and
21 he's going to further discuss study design
22 characteristics, including importance of sampling

1 and other study design considerations.

2 DR. BY: Thank you, Ebony. Good morning,
3 everyone. Again, my name is Kunthel By. I'm a
4 reviewer in the Office of Biostatistics in CDER.
5 So I'll briefly go over some of the design
6 considerations that we've outlined in the
7 discussion document.

8 You heard earlier that the purpose of Guidance
9 1, or at least we were tasked with writing a
10 document that provides or at least intends to
11 provide a framework for collecting patient
12 experience data that are not only comprehensive
13 but also representative of the underlying target
14 population.

15 And as representative is an important concept,
16 I'd like to briefly go over it, at least in terms
17 of how we've thought about it in the discussion
18 document.

19 So what is representativeness? Another way of
20 asking the question is what is a representative
21 sample and why do we care about it? Well, we care
22 about it because, in general, we cannot study the

1 entire target population. Usually there are
2 financial and physical constraints to do so. And
3 so, oftentimes we can only afford to study a
4 sample from the target population and we use what
5 we learn from that sample to make statements about
6 individuals in the target population.

7 And we would feel more assured about our
8 statements if we have a sense that the sample is
9 somehow representative of the target population.

10 So what is representativeness? In our
11 document, we interpret representativeness in two
12 ways. One, in the sense of generalizability and,
13 two, in the sense of representation. And I'll go
14 over each one of these in a few minutes.

15 The document does not insist on a particular
16 interpretation. The relevant interpretation
17 depends on your research objectives. So
18 generalizability, I think most of us are familiar
19 with this terminology.

20 But in our document, representativeness in the
21 sense of generalizability is when statements made
22 about patient experience based on your study

1 sample is generalizable to the target population.
2 That seems a little bit circular. But another way
3 of saying it is statements made about patients in
4 your sample is also valid for your target
5 population.

6 To illustrate, consider the following diagram.
7 I have a sample of 30 diabetic patients I
8 interviewed. And I characterized the distribution
9 of views and preferences with regard to treatment
10 burden among these 30 individuals.

11 Now, if these views -- if the distribution of
12 views and preferences are also true of the target
13 population of all diabetic patients, then we say
14 that the sample of individuals in our study is
15 representative in the sense of generalizability.

16 In terms of representation or
17 representativeness in the sense of representation,
18 patients in the study sample reflect the diversity
19 of patient characteristics in the target
20 population.

21 So in this interpretation, we do not insist
22 that the distribution of characteristics in the

1 sample approximate those in the target population.
2 In fact the distribution of these characteristics
3 in the sample could be very different from those
4 in the target population.

5 For example, in the sample diagram I gave
6 earlier, the sample of 3 0diabetic patients might
7 consist of similar numbers of blacks, whites and
8 Asians and similar numbers or proportions of young
9 and old.

10 But in the target population of diabetic
11 patients, there might be a substantial number of
12 whites relative to blacks relative to Asians and
13 there might be a substantial number of older
14 patients relative to younger patients.

15 So in terms of generalizability, we encourage,
16 or at least in the document we encourage the use
17 of probability sampling.

18 In our document, we enumerate examples of
19 probability sampling. I listed a few of them
20 here, which include simple random sampling,
21 stratified simple random sampling and so on.

22 However, we do not describe each of these

1 sampling schemes in detail. Instead, details of a
2 lot of these methods are provided through
3 references and we ask the readers to consult the
4 references.

5 One important feature of probability sampling
6 is that selection probabilities are known and, in
7 principle, reweighting of information in the
8 sample using these selection probabilities
9 provides a mechanism for generalizing to the
10 target population.

11 We acknowledge that not all studies will have
12 the goal of trying to generalize to the target
13 population and, for these studies, non-probability
14 sampling is often used. And representativeness in
15 the sense of representation is, or may be
16 sufficient.

17 In our document, we also list examples of non-
18 probability sampling schemes which includes
19 convenience sample, purposive sampling, quota
20 sampling and so on. And as with the non-
21 probability sampling, as with the probability
22 sampling, we don't go into detail in the document

1 on each of these methods. Instead, we refer the
2 readers or the literature.

3 What distinguishes non-probability sampling
4 from probability sampling is that the selection
5 probability or the selection mechanism is unknown.
6 So your sample may or may not generalize to the
7 target population. You just don't have a formal
8 way of making that determination.

9 As representativeness is an important design
10 consideration, so is sample size. Now, the
11 document does not instruct or provide formula on
12 how to calculate sample size, as that depends on a
13 multitude of factors, such as your research
14 objectives, the types of endpoints that you will
15 be using.

16 It depends on the study design, how you will
17 analyze your data, operating characteristics and
18 whether you will be paying attention to particular
19 subgroups.

20 In general, sample size calculation is based
21 on some sort of criteria. So establishing that
22 criteria is helpful, even if sample size formula

1 is not available.

2 Sampling frame goes hand-in-hand with
3 probability sampling. Essentially, it is a list
4 of members of the target population. For example,
5 to the extent that it is current, a disease
6 registry could serve as a natural sampling frame.
7 And ideally, you would want your sampling frame to
8 cover your target population, meaning to be
9 complete or near complete.

10 And having a sampling frame facilitates the
11 implementation of probability sampling in the
12 sense that you could apply some sort of random
13 device on the frame to pick out members from the
14 target population.

15 And we acknowledge that it's not always
16 readily available for us and to the extent that it
17 is possible to do so, sampling frame may need to
18 be created on the fly as you conduct your study.

19 And finally, whether your study is intended to
20 achieve representativeness in the sense of
21 generalizability or in the sense of
22 representation, we encourage enrollment of

1 patients that reflect the heterogeneity of the
2 target population, including diversity with
3 respect to demographic characteristics such as
4 age, sex, race and education, diversity in
5 cultural background, diversity in reading, writing
6 and speaking abilities, diversity in disease
7 severity and disease subtypes as well as diversity
8 in physical and cognitive abilities.

9 And before I hand it over to Michelle, I'd
10 just like to summarize some of the key takeaway
11 messages in terms of general considerations for
12 study design.

13 It would be useful to have clear research
14 goals and questions established, to have clearly
15 defined target population and to have -- to decide
16 in advance the type of information that you need
17 to collect to answer your questions, to decide who
18 will provide the information that you will need to
19 answer your questions and to decide how you will
20 achieve representativeness or which interpretation
21 of representativeness you will use and to decide
22 in advance how many people to include in your

1 study.

2 I think I missed one bullet point and that is
3 to include -- decide on whether you will be
4 looking at particular subgroups. And with that,
5 I'll hand it over to Michelle to begin the panel
6 discussion.

7 MODERATED PANEL DISCUSSION

8 DR. CAMPBELL: Thank you, Kunthel and Ebony,
9 for that overview of the beginning part of the
10 discussion document. So we're going to start with
11 some initial thoughts and feedback from our
12 panelists. And I'm going to start with Steve
13 Cohen, from RTI. So Steve, what are your initial
14 thoughts?

15 DR. COHEN: Michelle, let me make sure I've
16 got this on right. So I thought that the guidance
17 was a very good initial step in terms of framing
18 the broader context of data collection in terms of
19 the analytical questions at hand.

20 And I really like, particularly in figure two,
21 the strategic objective coming up first. Clearly
22 clarifying what the analytical goals of the study

1 are. What are the criteria of variables?

2 Sometimes there are competing objective and that
3 has to be factored in, in terms of ultimately what
4 are the priorities of the design.

5 Then, in terms of the guiding questions that
6 potentially could answer the research questions,
7 there was a framing of when they existed, when
8 there were very clear-cut, evidence-based measures
9 that might be taken from other surveys, nationally
10 represented, or they really have to be developed.

11 And that was the path in terms of considering
12 focus groups, non-probabilistic designs to really
13 engage small groups of patients with particular
14 chronic diseases or whatever the criteria would
15 be.

16 But for well-developed measures, being right
17 upfront in terms of what type of reliability is
18 necessary for this underlying study. If it's just
19 the overall estimate, it's what kind of a
20 confidence interval. If within subgroups that
21 you're trying to detect differences, what kind of
22 a difference can you detect?

1 What is the type one error, the type two
2 error, the power of the study? That's covered in
3 here and, as more references are provided, I think
4 that would be even more helpful.

5 The one thing that I think is really critical
6 here, when one goes through a well-designed study
7 with very clear-cut analytical objectives,
8 criterion variables well-specified, is
9 understanding when you're in the field, whether
10 it's in person or by mail or by phone, high level
11 of nonresponse in these studies.

12 And that has to be factored in the design.
13 Otherwise, even with the best frontend design, if
14 you have significant nonresponse and adjustments,
15 whether it's -- I'm going a little bit further in
16 terms of the guidance, but there are techniques
17 known as adaptive design, responsive design, to
18 get the representation up so that you won't be hit
19 with nonresponse bias.

20 And you have to factor that into the
21 underlying sample size specifications. If you're
22 only expecting like a 50 percent response rate,

1 you're going to have to double the underlying
2 sample that you need.

3 Then, another issue is the target population.
4 And that's really key. And many times, for select
5 populations, very difficult to get in a very cost-
6 efficient manner.

7 Now, there are national surveys that are very
8 large. There's the National Health Interview
9 Survey by CDC, which has over 100,000 individuals.
10 There's the medical expenditure provider --
11 Medical Expenditure Panel Survey.

12 On occasion, they add supplements for
13 individuals with particular chronic diseases. It
14 could be cancer survivors. It could be a
15 supplement for individuals with diabetes. To the
16 extent one can benefit by those existing surveys,
17 that's something that might be worth giving
18 consideration to.

19 And then, in terms of going forward,
20 pretesting is critical. Really taking out the
21 study first and seeing, you know, what the
22 pitfalls are in terms of it might be a beautiful

1 instrument, but it just doesn't resonate with the
2 patients.

3 And just the final point I'd like to make,
4 again, I'm maybe giving a little too much
5 attention to the fact that not everybody's going
6 to participate. Even when they participate,
7 there's item nonresponse and having mechanisms to
8 actually correct for that or see you're not going
9 to have sufficient representation. The question
10 doesn't work. So I'll stop there. But I was sort
11 of going over the field.

12 DR. CAMPBELL: Thank you, Steve. Richard,
13 would you like to start off with some comments?

14 DR. GERSHON: Sure. First of all, thanks to
15 the FDA and helping to bring patient input into
16 the 21st century drug development. And I'd like
17 to push that envelope even a little bit further in
18 my observations. Just a few quick examples. If
19 we have time later, we can dive in.

20 First of all, things like the HIV example
21 giving earlier suggesting, you know, group
22 discussions or administering surveys, we have a

1 new generation who actually would prefer to text
2 their responses or participate in social media-
3 based survey methods.

4 And indeed, that's a little bit in conflict
5 with discussion 3.1.1.2 regarding social media. I
6 believe the only way to talk to some of these
7 people will be that way.

8 And to preclude that is similar to our view of
9 phone-based surveys which we used to think was the
10 only way to get a random sample. And now, people
11 don't have phones. You can't get there.

12 So very often, I mean, social media can be
13 used, one, to get overall opinions in a non-
14 probabilistic way. But it can also be used as a
15 method to talk to known patients and experts.

16 Also relative to guidance on things like age,
17 you know, there's a growing body of literature
18 demonstrating that children are indeed accurate
19 self-reporters of health-related quality of life.

20 Things like the patient-reported outcomes
21 measurement information system has measures and
22 encourages self-report down to age eight. And

1 also, very interesting for drug outcomes or any
2 research, is to contrast that with the caregiver.
3 But that doesn't preclude the importance of the
4 child's input.

5 And also with regard to health literacy, I was
6 a little struck here that I think that, to me,
7 weak health literacy should be a requirement for
8 inclusion and not as a potential grounds for
9 exclusion.

10 Just because the patient can't understand,
11 read their medication instructions or understand
12 the prescription label, they can still be able to
13 accurately state their level of pain or emotional
14 status.

15 Finally, when we talk about probabilistic and
16 non-probabilistic sampling, I think the world is
17 changing and I think we need to recognize that
18 Web-based sampling may very well be non-
19 probabilistic -- or I'm sorry, probabilistic
20 sampling.

21 We're at this point where actually finding a
22 pure probabilistic population and being able to

1 obtain them, as was mentioned a few minutes ago,
2 there's response bias. Fifty percent of the
3 people don't respond and you don't get to them.
4 That is not a pure probabilistic.

5 I have yet to see -- you can get probabilistic
6 in a classroom of 30 children who all show up that
7 day and force them to respond. Short of that, we
8 certainly can't get that in a drug category.

9 So, and it turns out that things, Web-based
10 samples are being found by traditional groups who
11 always relied on probabilistic sampling to be more
12 representative, such as prediction of election
13 results. They're much more accurate when done in
14 a Web-based panel, when they're done with
15 traditional random digit dialing or other manners.

16 And further, things like we talk about
17 registries are limited by preregistered panelists.
18 Well, Web-based samples don't have to be limited
19 by preregistered panelists. There are different
20 types of web-based samples.

21 And in that regard, registries are also not
22 probabilistic samples. There is bias. I'm

1 unaware of a registry that contains a hundred
2 percent of the population. I think registries are
3 a great way to go. But they have a place, as does
4 Web-based sampling.

5 DR. CAMPBELL: Thank you, Richard. Meena?

6 DR. KHARE: Yeah. I'm Meena Khare, from
7 National Center for Health Statistics. I'm also a
8 survey methodologist. So I will give my opinion,
9 and thank you for inviting us for the panel
10 discussion.

11 I think Steve has covered a lot of ground and
12 comments that we also as a survey methodologist
13 look at it. Yes, and this document has covered a
14 very comprehensive list of all the required
15 things, concentration you should do.

16 So for the objective, yes, you have to have a
17 very clearly defined objective for what the stud
18 you are doing and how you are collecting because
19 that also could impact your target population. As
20 for the data collection questionnaire, as Steve
21 said, we have to do the pretest.

22 A question -- at NCHS, we have a questionnaire

1 design lab. Any surveys that we do, we always
2 test the questions and then sometimes there is a
3 measurement error that some questions may not mean
4 or they may not collect the information that you
5 want to collect.

6 So it's very important to do either a focus
7 group or some kind of testing or use the
8 preexisting questions that already have been
9 evaluated for data collection.

10 So that's on the objective part. And for the
11 representativeness of the target population, you
12 have to really look at what population subgroups
13 you're trying to target and where your data is
14 available because we do, as a household-based,
15 provider-based, establishment-based and all
16 different ways of method that we use for data
17 collection to get the representative sample.

18 So it's very important to start with the frame
19 and see where your subgroups are. If it's a
20 specific disease, where you're going to get the
21 collected data or find the patients, whether it's
22 a patient level or at the proxy or caregiver. So

1 you need to also think about the difference.

2 The caregiver may or may not be representing
3 your proxy information that patient might have
4 experienced sometime, especially when they talked
5 about the cognitive disability or something. So
6 you have to make a balance or do some kind of
7 quality assessment for that.

8 So, and data can be like collected from -- it
9 depends on how you're going to do sample survey,
10 clinical studies or from registries or nowadays
11 there's the medical records. Then you have to
12 think about it's the patient level, how you're
13 going to get the patient level data, experience,
14 directly from the patients or from the visit level
15 or providers or clinics.

16 Sampling methods and sampling size, as Steve
17 also said, that okay, you have to think about it.
18 Just having a random sample of 30 is not
19 sufficient all the time because you have to build
20 in the adjustment for the nonresponse, non-
21 coverage, missing data, item nonresponse, power of
22 the analysis, what kind of precision you want and

1 what kind of prevalencies in the population that
2 you're trying to target.

3 If it's rare, then you probably need to
4 increase the sample size quite a bit and we deal
5 with it all the time at NCHS. And I already
6 talked about the mode of data collection with
7 respect to objective and sample size.

8 Quality assessment I think as a pretest I
9 think it's good to do with some small study pilot
10 or some kind of partial data before you go into
11 the field for full data collection and like pilot
12 to do the assessment and make some changes,
13 quality improvement in your data collection
14 methods.

15 For the probability and nonprobability, yes,
16 we have an issue with the response rate. Response
17 rate, they all have a response bias issue when you
18 have -- but nonprobability nowadays, we are trying
19 to collect in multimode data set with the
20 multistage surveys.

21 There is a mode of fact there when you have a
22 -- and we are trying to get data from all

1 different methods. In one of the surveys that I
2 recently worked with, it was a mail from the
3 providers.

4 Also we gave them the option for Web and
5 telephone. And guess what? It was a very low
6 response rate for that particular study. But most
7 of them returned the mail survey. Web surveys is
8 still not there. And then telephone, for some
9 reason, telephone follow-up, very few data we got.

10 When I looked at the Web surveys, it's very
11 important to look at what is the demographic that
12 you're trying to focus. When I looked at it, the
13 younger group and the elderly, they are not that
14 Web savvy person with social media, savvy people.

15 But when you do some survey for young adults,
16 yes, that is one way to do it. So there are a lot
17 of issues going on with Web panel surveys. Yes,
18 is there -- a lot of the panels are increasing in
19 size and you can do stratification by demographic.

20 But it still is not there. There are a lot of
21 self-selection bias issues. So that's where I'm
22 going to stop.

1 DR. CAMPBELL: Thank you, Meena. Liz, would
2 you like to add on to this conversation.

3 DR. PIAULT-LOUIS: Sure. So, Liz Piauult-
4 Louis, from Genentech. So first, thank you for
5 having me here. I would like to also commend the
6 chair of this panel because I think this is going
7 to foster better patient-focused drug development.
8 And those guidance I think are really key for
9 collecting good patient input to inform the
10 assessment of clinical benefit for novel
11 treatments.

12 So I have two general comments. I think
13 within drug development program, we are not
14 interacting with the patient only at one point.
15 We are aiming at interacting with the patient
16 community and their caregiver or patient advocacy
17 group throughout the drug development program.

18 And that means that at the beginning we are
19 going to seek insight regarding the disease
20 burden. Then, we are going to try to better
21 understand how do we document this concept that
22 makes sense to inform clinical benefit so that we

1 can use this information alongside documentation
2 of treatment activities. And very importantly, we
3 need to also have feedback our protocol and on the
4 feasibility of this administration and so on. And
5 eventually, we are looking also for exit
6 interviews so that we can learn about the patient
7 experience throughout the clinical trial.

8 And for that, we are often relying on
9 convenience sampling or purposive sampling. We
10 need to have -- we have obviously like some
11 targeted questions. But we need to have a
12 relatively small sample and basically random
13 sampling won't be feasible at this time.

14 And then, we have also other type of research
15 when we are trying to develop a questionnaire.
16 And for that, we have also like other
17 opportunities then.

18 Only random sampling, we are usually using
19 purposive sampling and we are matching that to
20 specific target or equipment where we are
21 targeting certain proportion in terms of race,
22 education, physical functioning, communicative

1 ability and so on.

2 So it's really like a tradeoff about like
3 being able to get these patients inside to be able
4 to ensure the nice flow of information between the
5 patient advocacy group and the research team and
6 at the same time making sure that we can use the
7 information to inform all drug development
8 program.

9 And for that, I understand that we have to
10 have like -- I mean, we have to have -- we need to
11 be able to generalize the data.

12 But we have also other mechanisms when we are
13 doing, for instance, concept elicitation or
14 communicative debriefing. We have this concept of
15 concept saturation where we do make sure that
16 having more interviews is not going to give us
17 more information.

18 So that's help in terms of the
19 comprehensiveness of the feedback being collected.
20 So that's my comments regarding of course this
21 gathering of information from the patient
22 perspective, having clear questions make sense.

1 However, again, in early drug development
2 process, we don't have so much information
3 available. Most likely, if we are looking at a
4 rare disease, we don't have a clear profile of the
5 final target population for the Phase III trial.

6 So we have to be -- we are doing like a
7 hypothesis at this time. So we need to make sure
8 that the guidance -- I would encourage the FDA,
9 the draft guidance that is not too prescriptive
10 because we need to make sure that we have a nice
11 flow of information.

12 My second comment will be about this guidance.
13 I think we are currently at the industry
14 collecting this type of information early. But we
15 don't submit that to the FDA yet because we have
16 no clear understanding on how this is being used
17 by the FDA.

18 So I know that there is some discussion coming
19 in March on how to submit this type of information
20 to the FDA. But I would really recommend for this
21 guidance FDA to tell us how they intend to use
22 this information to inform the risk-benefit

1 assessment because we collect this information in
2 early phase of protocol development.

3 We do also have lots of patient-relevant
4 endpoints in our clinical trial. And what we see
5 so far is that we submit that to the FDA. We are
6 told that it is part of the treatment benefit
7 assessment. But unfortunately, we don't see that
8 in the label.

9 So we are I think trying to better understand
10 how we can use this new section in the patient
11 experience label and really trying to understand
12 the evidentiary standards that are applied to the
13 type of research we are discussing today. Thank
14 you.

15 DR. CAMPBELL: Thank you. So, Liz -- and I
16 just want to recap some of the themes I heard our
17 panelists discuss is their initial reactions. I
18 heard the need for considerations and using of
19 pretesting before we administer the survey out.

20 The use of social media, and I know that will
21 be touched on a little bit in our next session.
22 The considerations for nonresponse. How can we

1 potentially use large survey data that may exist?

2 The use of the reporter, who is the reporter, what
3 type of information will they be giving and how
4 they may complement each other.

5 And remembering our demographics and how that
6 relates -- of our population, how it relates back
7 to our research question and that we are working
8 continuously in our -- in our -- for our industry
9 members, they are continually working on the
10 patient experience concept throughout the entire
11 medical product development cycle and that one
12 method that some people are exploring to continue
13 to learn on the patient experience is exit
14 interviewing and wanting to know, as we move
15 forward with this guidance and other documents, is
16 how is the FDA using this patient experience data
17 towards making the benefit-risk framework in
18 decision-making.

19 So those were some of the themes I heard from
20 our panelists. I am now going to put up a couple
21 of questions to start with, with our panelists.
22 And we're going to start with the first one: are

1 there any other factors to consider when defining
2 research objectives and designing studies to
3 collect patient experience data that should be
4 included in the guidance.

5 I'm actually going to start with Suzanne
6 Vernon, our patient advocate's response. She
7 wrote a really great response and I want to make
8 sure her voice is still represented today.

9 And so, while our panelists continue to think,
10 we need to remember one of the things that Laura
11 Lee put in her slide that I know we talked about
12 on our prep calls with our session, is that we
13 need to make sure we're finding the correct
14 balance and the voice in what we're describing in
15 the guidance. You know, and so this is the
16 opportunity to let us know is there things we need
17 to add, where we may need to put more information
18 and take some stuff out.

19 So keep that in the back of your mind as
20 you're thinking, to our audience, to our panelists
21 today. We need to make sure we are making this
22 document broad enough to be useful and providing

1 the right level of information. So while our
2 panelists are thinking about that first question
3 on this screen, this is from Suzanne Vernon, who
4 again is from the Bateman Horne Center for MECFS.

5 I will note that Suzanne refers to a specific
6 figure in her talk, her thoughts. It's figure
7 three, and that is the nice arrowed figure that
8 Ebony showed that kind of talked about the flow of
9 the discussion document and how Ebony talked about
10 I think the first one through five steps in
11 session three.

12 She referenced that diagram. So if you hear
13 me say that, that is the diagram she was
14 referencing. So these were the words of Suzanne
15 Vernon.

16 First, you need to go in with your eyes wide
17 open. Let me start with a personal story. When I
18 was a young scientist at the Centers for Disease
19 Control and Prevention, I jumped at the
20 opportunity to lead a pathogen discovery study for
21 chronic fatigue syndrome because this disorder was
22 a blank slate and there was ample opportunity for

1 discovery.

2 However, despite the high prevalence,
3 debilitating nature and profound unmet needs of
4 CFS, few scientists or physicians believed this
5 disease -- that this was a disease and worthy of
6 research. This makes obtaining substantive
7 funding and publishing an uphill battle.

8 Fast-forward 20 years. Defining research
9 objectives and designing studies for CFS, now
10 called myalgic encephalomyelitis, or chronic
11 disease syndrome, MECFS is still stifled by the
12 multiple case definitions that have not been
13 operationalized, lack of funding, absence of
14 validated objective markers and lack of interest
15 from the pharmaceutical industry.

16 In order to make progress, it is essential to
17 start research about the patient experience with
18 establishing partnerships.

19 So for step one -- and this again refers to
20 figure three -- should be, one, establishing
21 partnerships that include patients, caregivers,
22 advocates, clinicians who manage the disease,

1 multidisciplinary team of scientists, regulatory
2 experts and peers. Note that this will be a lot
3 of upfront cost. But in the long run, it will pay
4 off.

5 The second step in figure three should be
6 working with your partnership team, understand the
7 condition. For example, is there a case
8 definition. Is there an ICD-10 code? Is that
9 natural history of the condition known? Are there
10 objective markers? So understanding better.

11 Once these essential steps are in place, the
12 research objectives and questions can be more
13 easily defined.

14 When working with patient organizations to
15 leverage their constituent populations and
16 decrease cost, patient organizations have very
17 vast reach for social media and can help
18 researchers reduce recruitment cost.

19 Understand the degree of disability caused by
20 the disease and understand that many with various
21 medical unexplained diseases and work with
22 clinicians that accept SSDI. Engage community and

1 indigent clinics and hospitals to help obtain
2 representative input from target populations.

3 Wherever possible, use open-ended questions
4 and passive data collection to ensure
5 representative input. Patient and symptom
6 heterogeneity and ceiling effects impact validity
7 and generalizability of survey questions in
8 standardized questionnaires.

9 As a patient's experience with their disease
10 is personal, I would like to see a greater use of
11 artificial intelligence and natural language
12 processing sampling methods to obtain more precise
13 and representative information about the patient
14 experience.

15 And again, those were from Suzanne Vernon, who
16 was our patient representative, who was unable to
17 join us today. So turning to our panelists who
18 may have had some time to mull over this first
19 question, I will start with Steve. Do you have
20 any initial thoughts on what other factors we
21 should consider?

22 DR. COHEN: I do, Michelle. One is, is this

1 data collection, this enterprise primarily for
2 monitoring, for establishing a baseline or is it
3 going to be impactful to actually facilitate
4 change.

5 So the question is who is the end-user. Is it
6 information back to the patients? Is it to the
7 medical community? Is it to legislators?

8 So being right up front in terms of who the
9 users are, the timing of it and that will clarify
10 whether or not it actually would be useful to go
11 forward if you can't get the information in the
12 hands of those who could make a change fast
13 enough. So those are things that would be key to
14 consider.

15 DR. CAMPBELL: Richard?

16 DR. GERSHON: Yeah, two things. One is I
17 think it was Suzanne's comment on passive
18 mechanisms of data collection. Recent research
19 has shown that analyzing movement data is a better
20 predictor of depression status a year later than
21 given a depression questionnaire or a clinical
22 depression examination. There are -- and that's

1 simply -- that unfortunately can be analyzed just
2 by looking at information gathered by your
3 cellphone provider or by an app that's put on a
4 phone, without getting an active survey being
5 answered.

6 Also I believe it's going to be next year or
7 the year after that there's going to be more
8 discussion of the measures themselves. But I'd
9 like to put forward the thought that quickly
10 developing an instrument, getting a little survey
11 data on it or some clinical interviews with people
12 does not guarantee you a reliable measure.

13 I kind of liken it to the person who uses
14 their relative who thinks that they have a good
15 sense of homecare to be their interior designer
16 versus a survey expert. People spend three to
17 four to five to 10 years developing survey
18 measures that are highly reliable.

19 And yet, you can go anywhere and find somebody
20 that says I can have that survey ready by
21 tomorrow. There's significant differences in
22 reliability. The other part of surveys in general

1 is that there's been a historical preference for
2 very specific disease-based survey measures.

3 And I'm struck by CMS's observation that only
4 30 percent of their patients have zero or one
5 condition. Therefore, when you ask a patient who
6 has a specific condition about their level of
7 fatigue, they're not giving you the level of
8 fatigue relative to this particular trial.
9 They're giving it also relative to the fact that
10 they have diabetes or something else.

11 And so, spending a lot of time narrowing down
12 that measure to do this one thing is just not
13 well-informed.

14 DR. CAMPBELL: Meena?

15 DR. KHARE: Hi. I think I covered pretty much
16 all the answers to those questions. A couple of
17 things I think I had missed is, again, when you're
18 doing it, look for also some of the availability
19 of data to benchmark or compare your estimates.
20 And if it's a disease as specific as Richard said,
21 yeah, you have to look at the whole profile.

22 In National Health and Nutrition Examination

1 Survey, we have an interview where we ask for
2 self-reported data and then also follow up with
3 the examination. And then, we can correlate any
4 specific disease that we follow in the enhanced
5 data.

6 Another thing, I think we already have covered
7 the mode of data collection. It's very different.
8 And then also look at the nonresponse bias and
9 non-coverage, all those representativeness.

10 One thing I missed saying is very, very
11 important for us as a survey agency is the
12 disclosure review. We have a disclosure review
13 board.

14 So when you release the data, I think we have
15 to be very careful that we do not identify -- as
16 an NCHS survey methodologist, we look at it and
17 not identify not just the patient or caregiver or
18 who is the respondent, also the manufacturers or
19 any other establishments because sometimes in the
20 rare disease situation, you might have a very
21 small group of people who are using it. So those
22 are other considerations we look at.

1 DR. CAMPBELL: Thank you. Liz, do you have
2 anything else to add?

3 DR. PIAULT-LOUIS: Yes. So for question one,
4 I think in terms of a research objective, we
5 should be -- we should not be afraid to be -- we
6 need to define those research objectives. But we
7 don't have to be too specific. And I really
8 encourage the FDA to think about the spectrum of
9 research we can do throughout the drug development
10 process.

11 So at the beginning, we don't have so much
12 information. And we need the breadth of
13 information. So we need like very general
14 objective, which is understanding the disease
15 burden, understanding the treatment burden, what
16 is the clinical benefit for the patient.

17 So those very broad objectives versus when we
18 are further along when we better understand the
19 disease and when we are like having interaction
20 with the FDA, then we can be much more specific.
21 We want to understand this specific function or we
22 want to understand this specific symptom evolution

1 over time.

2 So to me, it's like trying to find the balance
3 throughout the drug development process, not
4 relying on one study, but designing multiple
5 studies so that we could ensure that there is a
6 nice flow of information between the decision-
7 maker, between the patient experiencing the
8 disease and between a researcher designing the
9 studies to provide patient with new treatment.

10 DR. CAMPBELL: Thank you. So let's talk about
11 the third one, the third bullet. I'm going to
12 jump around a bit to keep us on our toes. And
13 we've talked a little bit about using the
14 probability-based methods.

15 But what situations do you think it's more
16 important to use that, the probabilistic-based
17 methods, and maybe in what situations it may not
18 be as important and what are some pros and cons
19 from that and what information could we gain. So
20 I'm going to start with Meena. Do you have any
21 thoughts on that?

22 DR. KHARE: As we do in the survey, I think

1 the first question is what situation is important
2 for sample patient using probability-based method.

3 We use most of the time probability-based
4 method because you have some frame information and
5 you can do -- you know the probability of
6 selection and you can adjust the data after
7 collecting and then how to weight it and how to
8 get the weighted estimate.

9 When it's less important, nowadays we are
10 talking about a lot of nonprobability sampling
11 because sometimes data collection, probability-
12 based method, multistage registry or face-to-face,
13 whichever way or multimode you do is very cost-
14 prohibitive and also the nonresponse is going up.

15 So then, look at the alternate options. And
16 there is a lot of literature also, how to combine
17 two different sources of data. So those other
18 research can be looked at, even though you have a
19 nonprobability and probability. There's a lot of
20 recent research that is going on. So that will be
21 a gain.

22 Loss is -- I think it's again going back to

1 nonprobability surveys, is what is your target
2 demographic because it's very different from
3 demographic and there is a lot of literature right
4 now coming up on Web-based panel.

5 I mean, so I looked at the data, the National
6 Health Interview Survey is address-based. So it's
7 total population. But when you start comparing
8 the people who said, yes, I use the Internet and
9 people who said I use the cellphone, only -- there
10 are differences.

11 So you need to make sure you evaluate your
12 estimates or findings. And then, timeliness is
13 another thing, how timely your specific disease
14 that you need the data to be disseminated or
15 estimate.

16 DR. CAMPBELL: Richard, do you have any
17 thought?

18 DR. GERSHON: Sure. Do we have an hour? I
19 think two things. One is that we use probability-
20 based sampling so we can project on what a
21 population or to get normative information. And
22 very often, we use it to keep expenses low and do

1 power analyses.

2 I think that what's known as non-probabilistic
3 methods very often are a lot less expensive and I
4 probably would rather have 20,000 people collected
5 from a non-probabilistic model than 30 people
6 collected from a probabilistic model. And I don't
7 use that number flippantly. I was able to collect
8 12,000 people on the Internet in a 48-hour period.
9 It took me another six weeks to get completely
10 balanced by demographic information.

11 Now, is it -- are there biases in that sample?
12 Yes, there are. Were those biases probably less
13 than any traditional model of gathering
14 probabilistic data? Probably were less, because
15 as Meena pointed out, there is no model of
16 reaching anybody.

17 And while I agree that getting young people on
18 Web-based is now a problem, that's because they're
19 already passed the Web. They're already ahead of
20 us. Okay? You can get them on Facebook, although
21 Facebook is not so much. They're on Instagram.
22 They are responsive. Indeed, they're much more

1 responsive than others. But trying to figure out
2 what method they're using tomorrow is really going
3 to be our challenge into the future.

4 DR. CAMPBELL: Steve, do you have any
5 additional thoughts?

6 DR. COHEN: Yeah. I see some opportunities
7 clearly in what's known as hybrid designs. But
8 I'd like to -- in the air -- I'm not Pablo
9 Picasso. But think of a bull's eye.

10 And while Richard gave an example of something
11 like 20,000 observations, think of an arrow that
12 really misses the target completely but's
13 incredibly precise versus the 30 sample size I
14 think was really unfortunate because if you had
15 something like maybe 2,000, 3,000, it might be
16 more scattered. But it would be more likely to be
17 in the center if you took the average.

18 So I have to say there is a whole theory
19 that's been developed in terms of probability
20 sampling. So one can make inferences. If one
21 could get the sweet spot of where this
22 representativeness is from the Web-based survey

1 and have like a dual frame design and a lot of
2 research is going into that area.

3 I think this is maybe behind the guidance.
4 But I really like that FDA is very receptive to
5 innovative methods and it isn't one size that fits
6 all.

7 But right now, it's to completely depend on a
8 non-probabilistic sample, unless it's really at
9 the beginning of like coming up with like a focus
10 group and measures development, I would still be
11 more supportive of probabilistic methods.

12 DR. CAMPBELL: Richard, do you want to --

13 DR. GERSHON: I would. I'm suggesting that
14 you can use Web-based data collection as a
15 probabilistic model, that it is -- it has all the
16 same pros and cons as a frame, as a registry so
17 that -- so yes, no, I'm a big believer. I don't
18 want to leave here thinking Richard Gershon
19 doesn't believe in probabilistic models. I do.

20 I'm just thinking -- I believe firmly that you
21 can -- there is no single way of getting the
22 people on that registry and the Web may just be

1 very well a way to get that or consider it a
2 registry in many cases.

3 DR. CAMPBELL: Liz, do you have any thoughts
4 on this and the considerations that you may have
5 to think about from your side?

6 DR. PIAULT-LOUIS: So I'm going to take the
7 opposite view. So I think probability-based
8 method is quite attractive because it decrease the
9 novel authenticity. That I could not agree more.

10 However, I think when we are looking to inform
11 the patient experience, we might not need those
12 large samples or to collect to such an extent to
13 make sure that we have a random sample.

14 I think throughout drug development, again, we
15 are focusing largely on purposive sampling, so
16 that it could be representative of our clinical
17 trial population. We have some limitation, of
18 course. We have some bias, like any research.

19 And I think if we are clear of we're getting
20 those limitations, those biases when we do
21 interpret the results, I think we should again
22 rely on what is practical, what is feasible to

1 give us the information we need to make decisions
2 for our drug development and for feasibility
3 assessment.

4 And again, I want to sort of emphasize that
5 there are some framework we can use for purposive
6 sampling. Again, recruitment targets. Again,
7 making sure that we do document situation of the
8 concept.

9 I also want to emphasize that most often, we
10 don't know so much about the population. So we
11 don't have all those AP data available. So we
12 need to keep an open mind so that we define our
13 objective and with that the limitation of the
14 findings.

15 DR. CAMPBELL: Okay. I'm going to turn over
16 to my panel on my left side, your right, and see
17 if there was any clarifying questions from what
18 they've heard today they might want to ask our
19 panelists, deeper thoughts. Laura Lee?

20 DR. JOHNSON: So I guess I have a couple of
21 thoughts and comments. And I'm going to start
22 with something that Richard said in his opening

1 which is interesting because we were actually
2 hoping to go where you went. And so, I'm worried
3 that it was misunderstood.

4 And so, part of what we're interested in is
5 actually seeing people with low literacy be
6 included so that they are not excluded so that --
7 this was misinterpreted by you as important
8 information for us as we start writing that
9 Guidance 1.

10 Another couple of comments pertaining to some
11 items that Liz brought up, I'm also thinking not
12 everything that is being collected needs to be
13 submitted to FDA. And so, thinking about kind of
14 what to submit, I would say that when a decision
15 needs support, that is -- so a lot of work happens
16 in all of research.

17 But not everything comes into the agency. And
18 when trying to parse out what to submit or not is
19 that, you know, if you're making -- if you're
20 asking for a decision that probably needs that
21 extra boost from us seeing that information, that
22 would be where I would focus on what should

1 actually get submitted.

2 Another element is that not everything is
3 going to go into the label. A lot of information
4 comes in and is considered, but doesn't actually
5 go into labeling.

6 So if you want to know what that label is,
7 that's that sheet of paper that you pull out, like
8 you know, it's this big. You can barely read it
9 because it's such small font. But if you're
10 lucky, find it online where it's a much bigger
11 font.

12 That is what we in FDA call label or labeling.
13 And it's not everything is going to go in there.
14 But that doesn't mean the information wasn't used
15 to make a decision about what is going in there.
16 So those are a couple of comments and thoughts I
17 had while listening.

18 DR. CAMPBELL: Okay. Great. I'm going to let
19 my audience know that in a little bit, we are
20 going to turn it over to ask you if you have any
21 questions or comments you'd like to add to this
22 conversation. So you may start thinking about

1 them. We will transition over to you shortly.

2 But I wanted to touch with something that
3 Steve brought up about figure two. And to refresh
4 your memory on what that is, that is a box of
5 factors to consider when selecting a research
6 approach.

7 And it has -- it's eight boxes and it talks
8 about your research goals or questions, your
9 target population, what type of information you
10 want to generate, short- and long-term impacts,
11 the type of information that's most valuable to
12 achieve these goals, what is the expected impact,
13 the amount of time and then budget cost things.

14 And Steve brought up a comment that these are
15 often competing objectives, which is true. I
16 would agree, as a former researcher myself.

17 But how -- of those things to consider, what
18 is one that you would think that we need to make
19 sure that we don't miss, that because they are
20 competing -- and I'm not sure if I -- I don't know
21 if I want to hear budget because I feel like
22 that's always the answer I get.

1 But some of those, what are things we want to
2 make sure that, in the end, when we are putting
3 that final research question together and then to
4 move forward, that ones you take into
5 consideration is to make sure that you really
6 remember to check into that consideration.

7 So does -- I want to start with our panelists.
8 Do you have any thoughts of what that might be,
9 that you may have seen where it was forgotten?
10 Steve, do you want to start, since you were
11 talking about the competing objectives?

12 DR. COHEN: Yeah. I just want to say it's
13 very hard to just say one. I think, and that's
14 why you said, it all in figure two.

15 But I just have to raise one thing, because
16 Richard, you know, mentioned something that really
17 resonated with me in terms of the fact that an
18 individual who has a chronic disease has multiple
19 chronic diseases or multiple conditions.

20 And recognizing that in the study design is
21 perhaps one of the most challenging things in
22 terms of what you're trying to eke out. So

1 factoring that in.

2 But I would have to say the research goals and
3 whether it's going to be impactful and whether you
4 have the dollars to do it would be the three
5 things I'd look at first. And then, if all those
6 three resonate, then go forward with designing
7 what you could design.

8 DR. CAMPBELL: Does anyone else have any
9 considerations? Liz, do you have any thoughts on
10 --

11 DR. PIAULT-LOUIS: So to me, it's how do we
12 avoid duplication of information, right? Because
13 you eliminated the budget issue. I think we don't
14 want to have like five different groups doing the
15 same study, right?

16 So again, how do we make sure that we
17 collaborate, regulators, payers, patients,
18 industry, so that we could address those questions
19 within unmet medical need.

20 DR. CAMPBELL: Okay. Richard, do you have
21 some thoughts?

22 DR. GERSHON: I didn't, but I love where Liz

1 started with this. So I'm going to take it from
2 there. And that is that the opportunities for
3 team science and the opportunities to conduct
4 joint research studies is simply a missed
5 opportunity time and time again.

6 When I got into patient-reported outcome
7 measurement, I went to my first International
8 Society of Quality of Life Research, which is
9 where people hang out who want to develop survey
10 measures.

11 And I was struck that the NIH had funded 40
12 different studies of fatigue that were being
13 demonstrated. Forty. And when all is said and
14 done, from the patient's perspective, I'm
15 completely convinced that all of them measured the
16 same thing.

17 From the patient's perspective of course, they
18 weren't related to each other. There were not
19 correlating statistics between those measures.
20 And yet, we took 40 times, 40 x an amount of money
21 that could have been done in joint studies. And I
22 would -- it's an interesting thing to consider is

1 how much of the drug development process could be
2 more in terms of shared research, saving just a
3 ton of money and make this more efficient.

4 And I would hesitate to say that anything
5 could be prioritized or taken off this list. I
6 think they all have to be considered, maybe some a
7 little less than others. But couldn't really make
8 a decision without considering all of these items.

9 DR. CAMPBELL: Great. So I'm going to talk
10 about the second bullet because we've kind of
11 talked about this a little bit in other responses.

12 What are those other factors and approaches we
13 need to consider when we're looking now at a
14 representative input from our target population?
15 And I might add a little flare to that because
16 it's been brought up a couple of times now the
17 idea of the multiple chronic conditions, that when
18 we're going in, we're looking at one specific
19 disease, but the patient may have multiple.

20 And so, you know -- so what are some
21 considerations we need to think about now when we
22 are looking at developing that research question

1 and, down the line, that sampling frame to get to
2 that? So, thoughts? I know Richard, I see --

3 DR. GERSHON: Well, one thing on the multiple
4 conditions is that is the real patient set. And
5 every once in a while, I'll see something that was
6 only done in patients that had the one condition.
7 That's not representative, right? That simply
8 isn't. I mean, that just shows you found a small
9 group of people who only had one item and
10 therefore that's not generalizable at all.

11 I think the other thing is we are struck with
12 increasing ways of finding patients and of
13 determining populations and target populations.

14 And for instance, something I think that
15 probably should be added to the discussion
16 document is the advent of electronic data
17 warehouses that almost any hospital has, any
18 consortium of hospitals has and now super-
19 consortia of hospitals which that you can
20 literally find any patient with a given ICD-10
21 code or a given disease and find those people.

22 And depending on how those hospitals have

1 consented those patients, you can get a list of
2 those patients and contact them, and may be much
3 less biased than any opt-in panel, although I like
4 opt-in panels too.

5 DR. CAMPBELL: Steve?

6 DR. COHEN: That really resonates with me,
7 going to either physician offices and then drawing
8 a sample. You then need like multiplicity
9 adjustments, which you actually talked about.

10 But then, there are those patients, think of
11 those that have hypertension that are not
12 diagnosed. And you know, maybe they're not going
13 to get treatment. But they're a group that you
14 really have to worry about too because eventually
15 they're going to enter into the system.

16 So having some sort of a coverage and more of
17 a general, overarching sample that would allow for
18 false negatives to be included in. So that would
19 be, you know, recognizing whatever screening
20 device you have is not really capturing the entire
21 population. Hopefully that's going to be small,
22 but recognizing that.

1 DR. CAMPBELL: Meena, do you have any
2 additional thoughts?

3 DR. KHARE: I can just add, because at NCHS,
4 we do a lot of provider-based, which is hospitals,
5 providers, physicians and we have started looking
6 into the electronic medical records to do the
7 sampling instead of going into the office. So
8 that gives you more power to search and do.

9 So that's right now we are in the middle of
10 looking at it, the quality of it and at some point
11 it's not there yet because not all the hospitals
12 and providers are right now again collecting
13 electronic data.

14 But at some point in the next couple of years
15 or five years probably we'll be there and that
16 will be very helpful. The same thing with the
17 registries. It depends on what you're looking at.
18 Sometimes registries are not complete.

19 With my experience with national immunization
20 survey, we always tried to go back to the
21 registries. But it's not as complete as going to
22 the provider's office and contacting them. So

1 yeah, it's coming up. But probably we have to
2 consider that.

3 DR. CAMPBELL: Okay. So I'm going to take the
4 flip side of that. What about with our rare
5 disease or smaller population?

6 Is there anything that may be more unique or
7 some additional considerations when we're looking
8 at representativeness that we may need to touch on
9 or people think about?

10 DR. COHEN: I just think of somebody who's
11 lost their keys and then goes where the light is.
12 So given that it's so challenging and so rare,
13 some information might be better than no
14 information.

15 So if there was some ways of conveniently
16 getting at those patients, that would be another
17 time to be -- you know, the costs are so
18 prohibitive and any information you could get
19 would be valuable for the next stage, it's worth
20 considering.

21 DR. KHARE: Yeah. I will agree with Steve
22 that sometimes it's better to have some

1 information and we have done an analysis of our
2 data, some of the rare diseases.

3 So even if it doesn't qualify as releasing the
4 estimate, we do have to have a lot of
5 documentation that limitations there. Btu it's
6 good to have that, such as like when HIV
7 infections started among the general population,
8 not the high risk population.

9 And then, all of those sampling methods are
10 there, networking, snowball. But then you have to
11 document, well, that okay, what is the focus and
12 objective of that. So that is good to have that.
13 Thank you.

14 DR. CAMPBELL: Liz?

15 DR. PIAULT-LOUIS: I'm mixing my thoughts. I
16 think often we are talking to the patient at one
17 time and we have now digital health. We have the
18 Fitbit. We have the iPhone. I think we do have
19 opportunities now to follow the patient a little
20 bit longer.

21 So instead of having a large sample, why not
22 having a smaller sample, but follow this sample a

1 little bit longer so that you have data for like
2 10 days, let's say. And you're able to document
3 some of the variability in the symptoms. But
4 again, that requires not to have one method
5 fitting everything.

6 It's more like, again, it's a field of
7 research. So what is the objective? If it's to
8 get like the breadth of information, trying to mix
9 the method, qualitative and quantitative.

10 DR. CAMPBELL: Okay. So I am going to turn it
11 over to our audience in the room, if there's any
12 questions that you may have or comments.

13 I will open the floor at this time. We have
14 four microphones. I would ask that you at least
15 state your name so we know who you. And I will
16 start on this -- on this side and go this way, you
17 know, swear if I can. So gentleman, sir?

18 AUDIENCE QUESTION AND ANSWER

19 DR. DEGBOE: Hello. My name is Arnold Degboe
20 and I'm one of the patient science directors
21 working with AstraZeneca support in oncology.
22 Thank you very much, Michelle and the panel and

1 the FDA for organizing this. And this has been a
2 very beautiful discussion.

3 I think your last question will be a segue to
4 my comment and thoughts about what has been
5 discussed, that what you do in terms of when you
6 have a rare disease and in situations where you
7 have patients who have diseases that are diagnosed
8 very late and they have a very short survival.

9 For instance, pancreatic cancer, that patient
10 may come very late. He's diagnosed. Within six
11 months or sometimes three months, they are no
12 longer alive.

13 So I think we need to -- the discussion appear
14 a little bit to probably assume a lot of
15 idealistic situations where you have all the time
16 and the resources in the world. You can do a
17 standalone interview and all that, use that to
18 inform your trial and do everything.

19 I think we should also look at it from the
20 perspective that sponsors will respond to
21 incentives. People -- and not just companies --
22 would just not generate data but they don't really

1 know what it will be used for. Anybody who works
2 in PRO knows that.

3 Even slotted in questionnaires sometimes into
4 your trial can turn into a whole discussion and
5 with a lot of pushback about people asking what
6 are you going to use their data for. You are
7 already analyzing survival and all that. Why do
8 you want to use PROs or you are using too many
9 PROs.

10 So I think it's important that when patient
11 experience data is going to be generated in a
12 nontraditional way, you tie in some incentives.

13 And in that way, I think we should break the
14 data collection between data that you are
15 collecting to inform your trial design and data
16 that you are collecting when the trial probably is
17 already going on and you want to use that data to
18 provide an additional layer of interpretation of
19 the data.

20 When you break it that way, I think the second
21 one, in-trial interviews can come in. When you
22 have a very rare disease where the population is

1 few, you may not have the time to interview those
2 and inform your trial. You have to do both
3 concurrently.

4 So in such context, whilst the trial is still
5 going on, there can be a simultaneous or
6 concurrent qualitative survey where you also
7 collect additional data about the patient
8 experience during the trial.

9 What made more sense to you? Are there
10 aspects of the assessment that should have been
11 done? What bothered you most? What were some of
12 the side effects that you never got the time to
13 discuss with your clinician?

14 And that kind of information can also be
15 considered by the FDA for the label. I mean, if
16 there were different modalities of treatment, some
17 were injection and some were tablets.

18 I think if the patient went through that kind
19 of experience and the drug is approved, new
20 patients may want to know about that, that
21 probably the oral form is preferable. And even
22 for the drug sponsor themselves, they might decide

1 let's go with an oral formulation rather than an
2 injectable.

3 So I think we should break this up into what
4 should be done to inform design and what should be
5 used and can be done concurrently during the
6 trial.

7 That way, we will be able to come up with some
8 kind of incentive for sponsors to know that this
9 is just not an exercise you are doing again to
10 produce data that you don't really know what it
11 will be used for. But in that way, it can be
12 used.

13 So my question to the FDA and to the panel is
14 do you have plans to develop this in such a way
15 that sponsors will see the need to do that. Thank
16 you.

17 DR. CAMPBELL: Thank you, Arnold. I think
18 that was highlighted earlier about how we will be
19 using this data is something that we will be
20 discussing and trying to determine. And
21 obviously, we'll make that known once that
22 determination is. That's -- we know that's

1 everyone's important question everyone has, is how
2 will this information be used. Theresa, did you
3 want to add on?

4 DR. MULLIN: Well, I guess I think that we're
5 hoping sponsors also see the importance of
6 collecting this kind of information, even on their
7 own.

8 And that in the example that you offered, I
9 think you'd probably be planning quite early in
10 the target profile if it's an oral version versus
11 injectable or whatever other mode of delivery.

12 And so, I guess we are thinking that it's
13 information that will be very important to FDA and
14 very important to the sponsor.

15 We think that if you involve the patient early
16 enough and you involve endpoints that are
17 meaningful, if you involve them in thinking about
18 trial logistics, you may do better with avoiding
19 dropouts. You may do a better job of trying to
20 reflect what matters most.

21 You may do a better job of responding to
22 questions that health technology assessors may

1 have later when it comes to reimbursement, all
2 things that would imagine to, I would imagine, a
3 sponsor. So hopefully there is a win-win, if you
4 will.

5 We're certainly trying to make these guidances
6 accessible and easy and we're also trying to help
7 avoid reinventing the wheel as much as we can.
8 Liz asked earlier about that information. It
9 might be collected very early on that might just
10 really help gain insight about the disease, people
11 living with the disease and what it is like to
12 live with the disease and current treatment.

13 And although that may not support regulatory
14 decision-making per se, FDA is planning to build a
15 repository of things sent into us that maybe those
16 early qualitative studies by disease, that may not
17 only be valuable to the person, the company or
18 whoever conducted it, but would be very helpful to
19 others pursuing therapies to treat that disease.

20 So we're hoping to help you avoid redoing work
21 someone else has done that's available to make use
22 of.

1 DR. PIAULT-LOUIS: Yeah, and in my experience,
2 we would like to figure out like a path for people
3 to submit this information not only to support
4 drug decision-making process but to facilitate the
5 discussion between the agency and the sponsor at
6 the early stage when, you know, you are
7 encouraging us to come to discuss the study
8 design.

9 We would like to understand what -- you know,
10 how do we submit this information because we have
11 the -- we gathered the patient insight and we want
12 to be able to provide that to you so that our
13 discussion regarding the target population, the
14 treatment, the endpoint can be basically evidence-
15 based rather than only hypothesis.

16 But I do agree with my colleague. It's early
17 stage versus evidence generated to support
18 development.

19 DR. CAMPBELL: Great. Well, thank you. Next
20 comment?

21 AUDIENCE QUESTION: Hi. I'm Xia Ha (ph). I'm
22 a software engineer. So I had a question about

1 how the real-world data, real-world evidence
2 initiative compares or contrasts with the patient
3 experience conversation that we're having here.
4 How does it align or how does it differ?

5 DR. MULLIN: So there's a lot in the real-
6 world evidence, real-world data sphere there. So
7 if you look at what's focused on in 21st Century
8 Cures, most of that is observational.

9 But at the same time, I think as was
10 mentioned, a lot of information is in fact
11 available in electronic health records and
12 available in other areas that are considered,
13 quote, unquote, "real world".

14 So a lot of this does interface with each
15 other, either trying to find ways to interface
16 with people that our sponsors and other groups
17 might want to use and finding them period.

18 But then also, I think, you know, where this
19 data is collected, we talk to each other pretty
20 regularly. So our lead for that in the Office of
21 Biostatistics in CDER is Mark Levinson, who's the
22 division director for our safety division. And he

1 was chosen because they've already started in this
2 realm.

3 That's a really important part of what they do
4 in safety work and it goes well beyond Sentinel,
5 for those of you who know what that is. But an
6 important thing to consider is we do work together
7 and we all talk to each other.

8 So I don't think there's a lack of interface.
9 But it's more when we need to talk to each other,
10 we do have a lot of conversations.

11 DR. CAMPBELL: Thank you. So to the person in
12 the back wearing the red?

13 MS. MURRAY: Hi. My name is Mary Murray. I
14 work in industry. But I'm actually here today as
15 a caregiver for a young man with sarcoidosis and
16 while sarcoidosis is --

17 DR. CAMPBELL: Mary, can you speak up a little
18 closer to the microphone, please?

19 MS. MURRAY: Sorry. Okay. Is that good
20 enough?

21 DR. CAMPBELL: That's -- yes.

22 MS. MURRAY: Okay. So I'm here today as a

1 caregiver for a young man with sarcoidosis, which
2 is actually not a rare condition, but a certainly
3 subpopulation of it that's symptomatic is rare.
4 And so, he's a part of that subset.

5 And what I wanted to say was my big
6 observation here this morning is that there's a
7 very heavy concentration on kind of the
8 statistical strategies that we're employing and
9 the conversation seems to be around a study level
10 approach. You know, the target population, et
11 cetera.

12 But what's missing for me is how we're going
13 to be able to incorporate some of the patient
14 narrative data that hopefully we're collecting in
15 electronic medical records through shared
16 decision-making processes and motivational
17 interviewing and that type of narrative data.

18 And how are we going to have the capacity at
19 FDA to incorporate that in some of the decision-
20 making? And the other piece I wanted to bring up
21 was if this is study level, that seems to feed
22 into the issue that you were addressing before

1 about sort of the cumulative burden on patients.

2 If there is a lot of redundant -- essentially
3 redundant studies going on out there, those
4 redundancies have a big patient burden. It's
5 tissue. It's blood you're collecting. And to
6 answer the same question, you know, it's very
7 burdensome on, you know, us as patients who might
8 not have a lot of lung tissue to spare.

9 So those are the two questions I'd have.
10 Number one, how can we incorporate some of the
11 narrative data that hopefully we're starting to
12 see showing up in the electronic medical records
13 into this process? And number two, how can we
14 reduce the cumulative burden on patients?

15 DR. CAMPBELL: Thank you, Mary. So Richard,
16 you want to --

17 DR. GERSHON: Yeah. It's interesting you
18 raise that because I didn't comment on the
19 qualitative type methods outlined because I think
20 they're actually here in a lot of places in the
21 guidance.

22 They're discussed about, you know, statistical

1 methods for qualitative data, how we get the voice
2 of the patient, how -- so actually, to the
3 contrary, I'd actually argue that the qualitative
4 methods are nicely outlined. Very often, they're
5 forgotten.

6 So I'd actually like to compliment they're
7 there. But I will admit none of the panelists
8 chose to discuss them.

9 DR. CAMPBELL: Theresa?

10 DR. MULLIN: I'll just add to that that we do
11 see those as extremely important methods. But
12 what we've been trying to do -- and qualitative
13 and narrative anecdotal accounts are very
14 important and very powerful.

15 But they won't be a substitute for data
16 collected for a whole population in terms of how
17 we can use it in decision-making.

18 And so, we're able to use narrative data,
19 including extracted from, you know, interviews, in
20 a way to ogive us general insight about how
21 patients feel, the clinical context for regulatory
22 decision-making, a general sense of the burden of

1 disease and burden of treatment that are available
2 today.

3 But in these guidances, we've been trying to
4 see if we can provide a clear way for patient
5 advocates and sponsors and others to go from that,
6 which is still quite valuable and informative in a
7 general way, to trying to collect this as data
8 that can be used to actually measure the
9 performance of a particular product that's under
10 development or investigation.

11 So that's still very important to us. But we
12 are trying to take it further in a certain way
13 with these guidances, this being the first.

14 DR. JOHNSON: I also want to comment I am a
15 big fan personally of data reuse, I will say. But
16 I'll also say it is very hard.

17 Many times, documents that we think might be
18 in electronic health records aren't or they are
19 not in there in a way that it is easily usable and
20 accessible. And I say this both as someone who's
21 spent a lot of years in research hand from what we
22 hear sitting here.

1 So I would encourage patient, patient groups,
2 other folks who really have discussions about how
3 to maximize the ability for data reuse and to
4 think about the multiple different groups who
5 might need that.

6 That may be your payers of the insurance types
7 of companies. It might be regulators around the
8 world. It might be sponsors. It might be
9 researchers that are funded by a whole host of
10 different organizations.

11 So that's something to also consider because,
12 while being aware of that burden, it is also
13 something that many times it comes up because
14 there hasn't been appropriate consent or literally
15 the data can go in and it cannot easily come back
16 out. And that's a fundamental concern. But I'll
17 leave it there.

18 DR. CAMPBELL: Okay. Thank you. Sir?

19 DR. LEVITAN: Hi. Bennett Levitan, from
20 Janssen Research and Development. So many people
21 here may know there was a recent drug label that
22 had a novel section on patient experience data.

1 And many of us were excited to see this and I have
2 no doubt that part of the guidances in the future
3 will start outlining how to do this in a more
4 general sense.

5 But in the interim, do you see it appropriate
6 for sponsors to start drafting labels that include
7 their perspective on patient experience data and
8 benefit-risk assessment?

9 DR. PAPADOPOULOS: I think that's a great
10 question. I think that, you know, there's only so
11 much real estate in our labeling. And the purpose
12 of labeling really is to, you know, assist the
13 prescriber and, you know, in the safe and
14 effective use of a medication.

15 And so, it's not clear whether all patient
16 experience data actually belong in the labeling
17 and, you know, are there other mechanisms of
18 communicating and incorporating important patient
19 experience data.

20 So I think that that's something that's still
21 under construction. But we do want our labeling
22 to be patient-centric and to provide information

1 on the, you know, benefits and risks on topics
2 that are important for patients and their
3 decisions.

4 DR. LEVITAN: So this is an issue that came up
5 in a recent experience where we attempted to put
6 in some benefit-risk information that we thought
7 would be very relevant to a provider. But there
8 really wasn't a place for it.

9 What I'm trying to get to is I'm sure you'll
10 be addressing these points over the next couple of
11 years.

12 But in the interim, if a sponsor starts
13 putting together patient engagement sections and
14 benefit-risk sections of labels, would they get
15 rejected out of hand or would they start being
16 considered as potentially applicable?

17 DR. MULLIN: So Bennett, I think at this point
18 we're just going to take it as a comment that
19 you've made about the need to do that. And we'll
20 just note that it's something that's, you know,
21 identified as a desirable thing to address.

22 DR. LEVITAN: All right. That's fine. Thank

1 you.

2 DR. MULLIN: Thank you.

3 DR. CAMPBELL: Thank you. The gentleman in
4 back?

5 MR. WHITE: Good morning. My name is David
6 White. I'm a patient advocate and a kidney
7 transplant recipient. I'm relatively new to
8 research. I think this patient's been answered a
9 few times. But I'm not sure.

10 To what extent do the people who are
11 participating in the survey need to understand the
12 terminology that is used in drug development?

13 DR. CAMPBELL: Well, that is a great question.
14 Andi don't think it has been answered today. So
15 that was a great question.

16 So I'm actually to turn it over to some of our
17 methodologists on our panel to talk about those
18 experiences and what do patients need to know when
19 you're particularly testing surveys and the
20 correct terminology. So Richard, do you have some
21 initial thoughts?

22 DR. GERSHON: I think that it's -- I think

1 whenever we do survey models or methods, we try to
2 find -- create a survey that's understandable by
3 the lowest, lowest possible literacy level because
4 that's the only way to cut it.

5 Somebody who has a high reading level will be
6 able to figure out something that's more readable
7 at a lower level. And when we design surveys, we
8 actually put them through computer-based engines
9 that assess the readability and what grade level
10 it goes.

11 We're very often able to get adult surveys
12 down to a sixth grade reading level which, by the
13 way, is not that low relative to the U.S. general
14 population. And so, even going lower is helpful.
15 I think relative to vocabularies in general, a
16 word that would hit a vocabulary list is probably
17 too high a level to be on a survey.

18 So it would have to -- if you need a word for
19 a particular disease, you really have to define it
20 within the survey itself. But there's major
21 danger -- those types of items in a survey
22 typically get kicked out later on. A person

1 simply doesn't understand it.

2 So I think it is important to consider what
3 you're talking about. And this gets back to me
4 comment about anybody can write a survey. What we
5 found out later on, when that anybody wrote a
6 survey, the data's pretty poor later on.

7 So really getting some expert methodologists
8 in there and frankly following -- there's survey
9 guidance that is thicker than what this discussion
10 document is and how to create those surveys, how
11 to make certain that they're reliable, how to get
12 sufficient input just on the survey document that
13 will later be used in a trial.

14 DR. CAMPBELL: Liz, do you have any thoughts?

15 DR. PIAULT-LOUIS: Well again, providing that
16 we want to capture the patient perspective, we
17 need to ensure that this is an appropriately and
18 that we use patient advocate, patient as partner.

19 So at the end of the day, we generate evidence
20 that are meaningful and discernible and explain
21 the clinical benefit of a drug. So I think it's a
22 basic criteria to ensure that a patient or

1 responder are going to understand the survey, but
2 also the objective of the survey.

3 DR. CAMPBELL: So, and as Richard mentioned
4 earlier, there was talk about the qualitative
5 methods section that was in the discussion
6 document.

7 This is when you start talking to your
8 patients to say do you know what this word means,
9 what does it mean to you, to really try to
10 determine what is the correct terminology to use
11 because there is some understanding that people
12 with health conditions may understand their health
13 condition-related words.

14 But you do need a test to make sure that it
15 can be applicable across the boards. I didn't
16 know if anyone from my other side wanted to chime
17 in. I don't think so.

18 I've got two people left at the microphones.
19 You will be my last two speakers for today. And
20 then, while they're asking their questions, if our
21 panelists want to think of a final comment. So
22 we'll be wrapping up shortly. So, ma'am?

1 MS KWON: Hi. My name is Jeemin Kwan. I'm
2 with the diaTribe Foundation. We're a nonprofit
3 that focuses on diabetes based in San Francisco.
4 And my comment is surrounding the idea of
5 representativeness.

6 And I wanted to bring up the idea of making
7 sure that the actual patient experience data that
8 is being collected is representative of that
9 individual's experience. So I guess this is
10 coming from my own musings.

11 So for people with chronic conditions, I think
12 that often the burden of disease, it isn't a
13 three-month average. It isn't a month-long
14 average. It is really like a daily, day-to-day
15 sort of experience.

16 And so, with these sort of patient experience
17 collecting methods, I think it's really important
18 to make sure that the timing of the questions
19 being asked really gets to the timing of events
20 that you want to understand.

21 So I'm wondering what sort of consideration
22 has been given to this and, yeah, what your

1 thoughts are. Thank you.

2 DR. CAMPBELL: So I think the question had to
3 do with how do we capture in chronic conditions
4 the timing of events to the timing of how we're
5 asking someone to reflect back in their question.
6 So I don't know if anyone has any thoughts on a
7 way to handle that or -- sure.

8 DR. GERSHON: It's hard because -- and that
9 doesn't make it something that shouldn't be done.

10 But it does bring in electronic data capture
11 and having an app on a phone that allows a person
12 to respond to an event when it happens rather than
13 a week retrospective or a monthly retrospective or
14 frankly an annual retrospective of what occurred.
15 You know, a person's pain on average may be very,
16 very low. That doesn't make it almost unbearable
17 at 10 p.m. for a certain condition.

18 So I think this is where we're likely to be
19 able to use new methodologies and new data
20 collection methods to go there. But they're
21 really new. You know, I'm saying if you pick up a
22 textbook or a methodology book, there's nothing in

1 there about this area.

2 And the flipside is it's completely legitimate
3 and our current -- you know, the well-known
4 methods simply ignored that because we could get a
5 retrospective piece.

6 And by the way, that's very patient-based.
7 Many patients, when you ask them about their
8 experience over the last week, will truly average
9 it. And therefore, a daily event that took place
10 for half an hour actually doesn't get included.

11 And the other patient will skip the fact you
12 asked them about the week. They will zoom in
13 directly to their most high impact event and tell
14 you about it.

15 So I think that could be taken into
16 consideration and finding out from a patient and
17 also hopefully new methodologies allow a person to
18 report in real time, contact your research desk in
19 real time. Those are methods that are now
20 available. But we're really at the dawn of that,
21 but so --

22 DR. JOHNSON: And I want to comment a little

1 bit on that too. And I think part of what you
2 alluded to also goes into Guidance 4.

3 So some of it starts very early, trying to
4 figure out and talk to patients like what is it
5 that we really need to focus on and then, moving
6 on, eventually not just that timing but also what
7 is that ultimate endpoint.

8 So if you talk about averaging over a month or
9 something like that, realistically that becomes
10 the endpoint of the studies that we're interested
11 in and how we're going to actually analyze the
12 data that's come in on the trials. So your
13 question actually nicely touches across all of our
14 guidances actually.

15 But I want to second what Richard said. It is
16 also an evolving area. When can we be asking and
17 how -- what information can we get when we do
18 those asks. And that's going to possibly change
19 per patient population.

20 But there may be a lot to be learned within a
21 given population and also maybe across multiple
22 chronic diseases or in other areas that can then

1 be gathered and used.

2 And we've seen that in the past as something
3 that could move forward. But it is, I think,
4 thinking about what is it that patients care about
5 is -- and finding that out from them is a very
6 important element.

7 DR. CAMPBELL: And to add on to what Laura Lee
8 said, as that is a great question that we'll be
9 expanding over our course of guidances over the
10 next five years, we do have the patient -- the
11 roadmap to patient-focused drug development where
12 the first column of that roadmap really does
13 highlight that understanding of the condition and
14 when are events occurring and what does it look
15 like in that patient population.

16 So while we are still beginning our journey on
17 these guidances today with Guidance 1, that might
18 be a start in looking at that resources that is
19 already available on our website to helping us,
20 you know, really tie in what are the events that
21 are important to patients, when are they happening
22 so we can accurately make sure we're collecting

1 them. Elektra?

2 DR. PAPADOPOULOS: I agree. That was a really
3 great question, very thoughtful. And I think as
4 we're talking more broadly about gathering patient
5 input, we really do need to consider the entire
6 journey of the patient, you know, from the time
7 when they're diagnosed all the way through, you
8 know, to their treatment experience, et cetera.

9 And so, having patients -- you know, sometimes
10 we can't help but to have them recalled back to
11 provide that journey.

12 And so, it really -- and then, if you want to
13 -- if you're talking about development of an
14 endpoint on the other hand, you know, you might
15 want to minimize that burden of recall to maximize
16 the accuracy of the data that you're achieving.

17 And so, you know, this will really depend on
18 your purpose of your research.

19 DR. CAMPBELL: Okay. Our last question?

20 AUDIENCE QUESTION: Great. Two-part question.
21 One is maybe Meena, if you've seen any health
22 literacy being done in audiovisual manner so that

1 if you're looking for that sixth grade or lower
2 literacy level, does audiovisual make a difference
3 in the explanation.

4 I have family members who are in clinical
5 trials and some of them get the very long
6 explanations. But nobody -- I've never seen one
7 where they've actually had a video or something
8 explain that to them each time that they do the
9 entry.

10 And maybe Richard, you can talk a little bit
11 about -- we'll geek out for a second and talk a
12 little bit about conversational user interfaces
13 and how the chat bots and other interactive
14 conversations that you could have, instead of
15 asking a 40-question survey all in an hour, could
16 you ask those same 40 questions over a week and
17 get a better answer, more through, in an
18 interactive capability through SMS or chat bots.

19 So, and I mean, any one of you can answer both
20 questions. But I thought just anecdotally letting
21 us know what you're seeing in the marketplace
22 might be good.

1 DR. CAMPBELL: So before we have our extensive
2 conversation on chat bots, which sounds very
3 interesting, if we can get maybe a high level
4 response on that from Richard and then you guys
5 can connect during lunch on that.

6 But then, and let's not forget the first part
7 of the question is the uses of audiovisual aids to
8 help us in the health literacy when we may be
9 dealing someone with a low health literacy level.
10 So Richard, do you want to start?

11 DR. GERSHON: It's a very popular topic in
12 research right now, is burst designs and EMA
13 designs, which allow -- exactly focus on that.
14 Let's get people many, many times over the course
15 of a day versus a summary event or over the course
16 of a week and aggregate that data together.

17 So that's -- there's actually a lot of
18 research funding available right now to prove
19 that. I think it will be useful. I don't think
20 it will solve everything. It's literally the wave
21 of the moment if you look at funding that's
22 available for researchers in this area.

1 And I'm going to sneak into Meena's area and
2 respond for one second because I work with several
3 people who do health literacy research. And they
4 very often are providing surveys with a button to
5 have an auditory response along with it. And I
6 haven't seen anyone actually add video.

7 But that's a very neat thing where technology
8 is today, that to add that type of thing is much,
9 much less expensive than it used to be. So, and
10 we can talk about chatrooms and things like that
11 at the break.

12 DR. KHARE: For our surveys, in National
13 Health Interview Survey, I don't have the current
14 recent information. But in the National Health
15 and Nutritional Examination Survey where there is
16 an interview and then they come to the mobile
17 examination center, there is some audiovisual.
18 I'm not sure how much detail.

19 But then, there is the interviewers go through
20 extensive training to explain the terminology, the
21 definition and also they have hotkeys to explain.
22 And some of the time, we do use some audiovisual.

1 I don't know how specifically for certain disease.
2 But then, there is some because now they have
3 iPads and others things that you can bring it in,
4 which is not those days when you had a paper and
5 pencil or just a big heavy laptop.

6 But yeah, they do try to do it. But how
7 extensively, where it's feasible, because you have
8 to reduce the respondent burden and then
9 interviewers are trained and retrained to explain
10 everything that comes in the questionnaire. And
11 they are pretested. That's all I can add.

12 DR. CAMPBELL: All right. Well, great. So I
13 want to thank everyone from the audience for their
14 questions.

15 As we wrap up, if our panelists have one final
16 thought they would like to add that's not been
17 said or they've thought about, this is the
18 opportune time now to add anything. And if Ebony
19 or Kunthel have anything they want to add from
20 what they've heard today, this is the opportunity.

21 No? No?

22 So if there's no additional final thoughts, I

1 want to thank firstly our panelists for
2 participating today. I think we did a great job
3 and I think we had a great discussion. And we've
4 heard many things. My note pages are completely
5 covered. So I know I cannot do a good job in
6 summarizing.

7 But I think some key messages were the
8 possibility of collaboration and trying to reduce
9 patient burden through us doing multiple studies
10 of the same thing and working together.

11 What is the information in patient experience
12 data being used for? Is this being used to inform
13 trial design or is it being ongoing during what's
14 occurring during a clinical trial? And how do we
15 handle when a person doesn't have a single
16 disease, they have multiple diseases and what are
17 those considerations?

18 So I thank you again for listening. I thank
19 panel one. We will adjourn at this time for
20 lunch. Please be back at 12:30 for the remainder
21 of our afternoon session. Thank you.

22 (Applause.)

1 (Whereupon, the foregoing went off the record
2 at 11:33 a.m., and went back on the record at
3 12:31 p.m.)

4 MS. VAIDYA: Hello, everyone. We'll get
5 started in about two minutes, so if folks can
6 start settling in, thank you. Welcome back,
7 everyone. I hope you all had a nice lunchbreak
8 and enjoyed the bagged lunch that we had here.

9 We are now ready to begin our next session and
10 kick off the afternoon with session -- we'll have
11 three sessions in the afternoon actually. So
12 we'll start off with methodological considerations
13 for data collection, analysis and
14 operationalization.

15 I'll turn it over to Scott Komo, who will be
16 moderating session two, from the Office of
17 Biostatistics in CDER. Thank you.

18 SESSION II: METHODOLOGICAL CONSIDERATIONS FOR
19 DATA COLLECTION, ANALYSIS AND OPERATIONALIZATION

20 DR. KOMO: Thanks, Pujita. Hello. My name is
21 Scott Komo, from the Office of Biostatistics. I
22 was going to tell you I hope you had a nice lunch.

1 But apparently Pujita already handled that one.

2 So first, this is for our session on
3 methodological considerations for data collection,
4 analysis and operationalization. I'd like to
5 first introduce our panel. First is Dr. Kai
6 Ruggeri, who's the director of global research
7 analysis for population health at Columbia
8 University.

9 And next would be Dr. Steve Cohen, who's the
10 vice president at the Division of Statistical and
11 Data Sciences at RTI. And next to him is Dr.
12 Sheri Fehnel, who is the vice president of
13 patient-centered outcomes assessment at RTI. Next
14 would be Dr. Gary Globe, who's the director of
15 global health economics at Amgen. And last is Ms.
16 Isabelle Lousada, who's the president and CEO of
17 the Amyloidosis Research Consortium.

18 So I'd like to first give you a brief overview
19 of sort of what's going to happen in our session.
20 First, Selena Daniels, from the clinical outcome
21 assessment staff at CDER will present the key
22 concepts from the sections three and four of the

1 discussion document. Then, I'll quickly recap
2 sort of what was presented. And then, each
3 panelist will then give a short overview of their
4 initial response and reactions to the presentation
5 and discussion document.

6 Then, the panelists will then be asked to
7 address the questions that were in the -- that are
8 listed on the agenda. We'll then follow that up
9 with questions from the floor and finally we'll
10 wrap up the session. Okay. Selena, would you
11 like to come and please give your presentation?

12 FDA PRESENTATION

13 DR. DANIELS: Thank you, Scott. As Scott
14 mentioned, my name is Selena Daniels. Good
15 afternoon, everyone.

16 So in the previous session before lunch, we
17 heard some considerations on how to define
18 research objectives and design studies to collect
19 patient experience data. In this session, I'll
20 present some considerations on what types of
21 methods that can potentially be used to collect
22 patient experience data, including analysis as

1 well as some considerations on how to standardize
2 the data collection process.

3 So this slide should be familiar. These are
4 some general steps for conducting studies. The
5 last session focused on the first five steps and
6 the content I'll present in this session will
7 target the last three steps, first beginning with
8 considerations for methods of data collection and
9 analysis.

10 So this is an overview of the different
11 methods that can potentially be used to collect
12 patient experience data, which includes
13 qualitative, quantitative and mixed methods.
14 Qualitative methods can include the act of just
15 talking to people by using direct communication to
16 explore or confirm the meaning of interpretation
17 of a topic from the participant's perspective.

18 An example of a qualitative study may be just
19 talking to a group of patients to describe their
20 experience with their disease or condition. And a
21 potential scientific objective for this method
22 could be related to exploring the most important

1 aspects of that disease for your target
2 population.

3 Quantitative methods are characterized by the
4 collection of quantifiable data or the use of
5 numbers and apply statistical methods to summarize
6 the collected data. With regard to collecting
7 patient experience data, this information could be
8 collected by the use of a tool, for example, a
9 survey or a questionnaire.

10 And an example of a quantitative study may be
11 surveying a group of patients with a
12 questionnaire, allowing them to rate the severity
13 of their disease symptoms using questions with
14 response options to choose from to create a score.
15 A potential scientific objective related to this
16 method could be the development of a questionnaire
17 based on that patient input.

18 Lastly, mixed methods are where both
19 qualitative and quantitative methods are used. An
20 example of a mixed method study may be surveying a
21 group of patients with a questionnaire but then
22 also including an interview component which allows

1 patients to further describe their response with
2 more detail that may not have been provided with
3 those response options in a questionnaire.

4 And a potential scientific objective related
5 to this method could be determining whether
6 symptom severity or symptoms frequency is most
7 important to patients by looking at severity and
8 frequency scores but also looking at patient
9 quotes or patient narratives.

10 So overall, each of these methods can allow
11 one to understand patient experiences,
12 perspectives and feelings. And in later slides,
13 I'll break down these methods a little further.

14 So we have these methods, but how do we
15 determine which methods to use? Some potential
16 factors to consider in selecting a method
17 including the following, but not limited to,
18 research questions and goals.

19 So does your method address your question or
20 goal? Individual characteristics of the method.
21 Your target population, is your population
22 accessible for the particular method that you want

1 to use. And then, expected data, what type of
2 data do you want to produce from your study?

3 So I'm going to take a little deeper dive into
4 these methods. The key outcomes for qualitative
5 methods is to discover or explore rather than test
6 a concept.

7 Another outcome is determining the meaning of
8 and refining specific research concepts. And some
9 potential sources to obtain this data or these
10 outcomes includes talking to individuals.

11 You can talk to participants in different
12 modes or settings. For example, the use of
13 interviews. This could be one-on-one interviews
14 or these could be focus groups where you're
15 talking to a group of participants at one time.

16 It can be social media, as we discussed in the
17 last session. A consensus panel could also be
18 another approach. For example, a Delphi panel in
19 which you're talking to a group of experts to gain
20 consensus on a certain topic.

21 In regard to analysis of qualitative data,
22 there are some general steps that should be

1 considered which involves, one, compiling and
2 organizing data either through your notes, a
3 glossary to sort of see what kind of terms are
4 coming up and/or software; second, classifying
5 data by coding data, by creating themes or topics
6 that are coming about in the discussion;
7 interpreting data by connecting the data to your
8 research questions; identifying the main theme of
9 the data and/or patterns, if any; and lastly,
10 representing and visualizing data. And this is
11 considering how you would you present the data,
12 whether it's tables, pictures or graphics, et
13 cetera.

14 The key outcomes for quantitative methods are
15 to test, rather than discover, concepts. And to
16 obtain data to test, a source could be a survey or
17 a questionnaire. With regard to the analysis of
18 quantitative data, the analytic approach to use
19 should be appropriate for the research objectives,
20 the study design and types of data generated in
21 the study.

22 The key outcomes for mixed methods are to

1 discovery and/or test concepts. And the sources
2 used for both qualitative and quantitative methods
3 can also be used with this method. Likewise, a
4 combination of analyses for qualitative and
5 quantitative methods can be used as well.

6 So we know that there are different methods to
7 collect data. The next question becomes how can
8 we standardize this data collection process with a
9 method that is used.

10 This slide provides a brief overview of the
11 data collection activities that should be
12 considered to help operationalize and standardize
13 the data collection process. And these activities
14 are sort of interrelated, sort of like a chain, as
15 illustrated on this slide.

16 So first, beginning with locating patients and
17 sites, a critical step in the process of data
18 collection is to identify the appropriate sample
19 and/or sites to study.

20 For any study that involves gaining access to
21 sites and patients, one should seek permission
22 from a human subjects review board prior to

1 studying and comply with the institutional review
2 board, or IRB. And just like any clinical study,
3 a patient experience study should comply with good
4 clinical practice.

5 Next, the activity of sampling. You should
6 consider determining the strategy for sampling of
7 patients or sites. And we have been told about
8 the different types of sampling methods in the
9 previous session.

10 The act of data collection itself, you should
11 consider the most appropriate data collection
12 approach for the research objective. And once you
13 have collected that data, then how do you record
14 it. Recording that information, you should
15 develop written forms or protocols to collect
16 data.

17 And in an attempt to avoid or maybe resolve
18 site/field issues, you should consider providing
19 standardized training to research team members.
20 And lastly, data management and storage. You
21 should consider formulating a data management and
22 storage plan prior to the conduct of your study.

1 So in addition to standardizing data
2 collection activities, the reporting of results
3 should also be standardized to the extent
4 possible.

5 Materials that would help benefit FDA would
6 include, but not limited to, would be the study
7 protocol and this can include the interview or
8 discussion guide or the tools, if applicable, to
9 the method that you've selected, as well as the
10 study reports. And this may or may not include
11 transcripts, if it's applicable to the method that
12 is being used.

13 So there are some levels of detail that was
14 included in the discussion document that may or
15 may not have been presented extensively today,
16 which are located in the appendices.

17 And these appendices contain information
18 regarding the timelines for the development of
19 guidances, standards and requirements pertaining
20 to submission of data, best practices on
21 qualitative interviews, Delphi panel techniques
22 and characteristics, considerations for data

1 management and, lastly, some more information on
2 methods for collecting patient experience data.

3 And so, before opening up to the discussion,
4 I'll leave you with some key takeaways. Research
5 objectives/questions should inform the methods
6 that are used to conduct research.

7 The other factors to consider are the
8 individual characteristics of the method, target
9 population and expected data and, second, data
10 collection process, including data quality issues,
11 and reporting of findings should be standardized
12 to the extent possible. And I'll turn it over
13 back to Scott.

14 DR. KOMO: Thank you, Selena. Great. So that
15 gave us a nice overview of the methods that could
16 be used to collect data. These would include
17 qualitative, quantitative and mixed methods and
18 also how to determine which methods to use.

19 We also had a discussion on how best to
20 collect data and how the collection should be
21 standardized. Also we had a discussion on
22 reporting and how submitting the data to the FDA.

1 At this point, I'd like to call on our -- ask
2 our panel to provide a brief initial reaction to
3 the presentation and the discussion document.

4 First, I'll ask Kai Ruggeri, please, to --

5 MODERATED PANEL DISCUSSION

6 DR. RUGGERI: So, good afternoon. Thank you
7 very much. So first, I should say I'm a
8 behavioral researcher interested in the policy
9 impacts on population wellbeing.

10 So from that perspective, I find the guidance
11 document to be very useful, largely because I
12 think it does an excellent job on three principles
13 of public engagement, which is that it's salient,
14 it's simple and, most importantly, it's
15 actionable. So anyone who can read it can take
16 away what to do with that information.

17 I was going to make some comments about
18 generalizability, as mentioned earlier. But a
19 lot's been said this morning and I believe more is
20 coming. So I'll skip that part for now.

21 I wanted to focus on just one of the questions
22 that was asked to us which was about more or less

1 detail in the future, which is a big part of any
2 guidance document. I think more detail is always
3 fine.

4 I think the issue is to make sure that any
5 guidelines or frameworks remain salient, but where
6 further information is easily accessible and
7 clear.

8 So you don't want to miss out on the key
9 principles by just overwhelming with loads of
10 information because in many cases, when providing
11 these frameworks, we're talking about how to give
12 clear guidance and then how to make use of
13 information when we deviate from that guidance or
14 what to do when that happens.

15 And I speak about this largely because I was
16 asked to speak discuss -- or largely focus on the
17 qualitative side of things. One of the big
18 guidance that we hear a lot when qualitative data
19 is being generated alongside other studies or
20 quantitative data is that you don't want to just
21 repeat what's being captured in quantitative data
22 by interviewing people.

1 While I agree with that sentiment, there's
2 also a risk that you end up doing something
3 completely new that has no common denominator with
4 the quantitative data, and in which case you
5 wouldn't have complementary data. You would have
6 two separate data, pieces of data talking about
7 two different things.

8 So I think one of the main things in that
9 framework is to make sure that there's still
10 common denominators regardless of which type of
11 data or method are used. That way, what you have
12 continues to complement. And in this way, what's
13 ultimately important about any of these guidances
14 is that it should be very clear on what is the
15 purpose.

16 So before any data is selected or methods or
17 analytical approaches, the purpose has to be
18 clear. In my lab, we use four P's when we talk
19 about purpose: precision, prediction, pattern and
20 perspective.

21 The first three are really about deciding are
22 we trying to be incredibly specific with the

1 information and the analyses we're generating or
2 are we okay with a more broad, general
3 understanding. So we pick different analytical
4 approaches to the data that we have.

5 But when we start getting to prediction, we
6 start having to be much more specific and the
7 biggest distinction really between qualitative
8 methods and quantitative methods is prediction
9 because using qualitative data for prediction
10 would be a big problem. If that weren't true, my
11 family would never get into an argument about
12 where to have dinner.

13 But when we start shifting over to actually
14 wanting and desiring that individual perspective,
15 we start having to think of more structured
16 approaches to the qualitative. But the challenge
17 within that then enters into our area of research
18 which is heavily focused on bias.

19 So I'll just say a few words about bias, which
20 I think would be a very interesting topic to
21 consider within this, largely because when we open
22 up the qualitative methods, we acknowledge how

1 important the individual experience is and we're
2 saying this is critical in our decision-making.
3 But we're also opening ourselves up to the most
4 explicit form of bias, which is individual
5 narrative. And I don't say that in a bad way.

6 But I think it's something that has to be
7 understood. Some examples are when we ask
8 questions in open settings, we often ask them in a
9 way that's more likely to confirm what we already
10 think than it is to likely find new information or
11 to contradict what we may think of refute a
12 narrative.

13 In addition, because this is meant for an open
14 comment, do the people who are providing it
15 understand the decision-making structures of the
16 organization, because another form of bias is we
17 have the bias to think the insights we generate
18 and the narratives we provide are the ones that
19 should be actionable.

20 So taking into account these biases in
21 guidelines is always something important. We've
22 converted this into an ethics guideline for when

1 we generate data and run analyses. I won't go
2 through all of that now. But those are some of my
3 thoughts.

4 And I just would wrap up by saying really it
5 comes down to if it's ultimately clear to always
6 refer back to the ultimate purpose, then I think
7 it's a very useful thing, regardless of the extent
8 of detail or the specific frameworks provided
9 because being very clear about that purpose,
10 you're more likely to use the methods that are
11 aware of the biases you might have, but also speak
12 specifically to your objectives that were
13 mentioned earlier. Thanks.

14 DR. KOMO: Great. Thank you. Steve Cohen,
15 could you please give your thoughts?

16 DR. COHEN: Yeah. Sure, Scott. Thank you
17 again. I also thought this component of the
18 guidance was well-articulated. A lot of attention
19 was given to the qualitative methods.

20 So I'd like to focus more on the continuum,
21 moving from this morning from design aspects.
22 Again, we refocused on some of the issues in the

1 chain that Sylvia presented. It's also presented
2 in figure 12, is more of a linear continuum from
3 data collection to sample to then actually getting
4 the data in hand.

5 And from this perspective, having a very clear
6 set of what the analytical questions were, making
7 certain that the design actually had all the
8 ancillary information for controls in terms of
9 testing underlying hypotheses.

10 Many of the designs that would be required to
11 target some select population subgroups would
12 probably require quite a bit of oversampling to
13 meet some of the objectives.

14 And so, bringing in the adjustments to the
15 probabilities with selection, in many of the
16 analyses this is known as weighted, making
17 adjustments, and then further adjustments for a
18 complete nonresponse.

19 And there is going to be some Swiss cheese in
20 some of the responses and making a determination
21 of what is the lowest threshold for acceptability
22 and coming up with the correct imputation

1 strategies.

2 So then, you go forward with the analysis.
3 And having some -- a bit more reference in terms
4 of the analytical techniques that would help you
5 get the best precision in your estimates and using
6 the appropriate variance estimation strategies for
7 designs that don't necessarily follow a simple
8 random sample.

9 There are a lot of design complexities that
10 might be coming to the table. There's a term
11 known as a design effect which is the price you
12 pay in a way in terms of the loss in precision
13 relative to a simple random sample and to have
14 that in the underlying analysis platform.

15 So all along the way, recognizing that you
16 really want to inform what's going on. And to the
17 extent in the analytical strategy you could think
18 of ways to fast-track some preliminary estimates,
19 to get back to those individuals who have designed
20 the study and who were the sponsor of the study,
21 to point out some interesting unexpected results
22 or counterintuitive results.

1 Having early result, you know, and resonating
2 with that is very, very important. Having
3 transparency in terms of the analyses that were
4 done. So there's reproducibility. That's
5 critical.

6 So it's not like a black box solution that
7 comes out from the investigation, that you
8 actually -- it's well-documented. It's
9 reproducible. And then, thinking about the
10 questions in terms of how analysts would gain
11 access to the data.

12 There is a bit of -- quite a bit of attention
13 to protecting confidentiality. That's first and
14 foremost critical in terms of making sure you have
15 future participation for surveys, particularly for
16 longitudinal surveys.

17 But if there is a decision to make some of the
18 data available in the public domain, being very
19 aware of what's known as the mosaic effect, that
20 even by itself, this data might not be
21 identifiable. But with all of the information
22 that's in the public venue, there still might be

1 some methodology that would violate a
2 confidentiality protection.

3 So those are some of the things the guidance
4 addresses. Perhaps a bit more reference to some
5 examples there. And then, my final consideration
6 is that there is a wealth of ancillary data for
7 individuals with one or multiple chronic
8 conditions from national surveys.

9 And at a higher level of aggregation, they
10 could be used for additional analytical power.
11 And there's actually an effort. Actually, it was
12 presented at an FDA PDS symposium I guess about
13 two months ago. PDS is Project Data Sphere.

14 It's actually an enclave that has Phase III
15 clinical trial data that's available. It was
16 primarily the comparator arm of that, for a
17 particular clinical trial. Now, the actual
18 treatment arms are being made available.

19 For approved projects, researchers can get
20 into that enclave. So you have some of the data
21 from clinical trials. There's also some work now
22 supported by Robert Wood Johnson Foundation to

1 actually synthesized existing survey data for
2 cancer survivors for particular cancers, to do
3 statistical linkages to demonstrate some other
4 factors that perhaps might be insightful in terms
5 of from a nationally representative sample of
6 cancer survivors, who makes it into the trials.

7 The trials are randomized. But the
8 representation and the overall population
9 sometimes doesn't meet the representation that you
10 would see.

11 So making use of available data for synthesis
12 will give one additional power in terms of
13 prediction, but also facilitate additional
14 analyses that might not have even been considered
15 at the get-go. Thank you.

16 DR. KOMO: Thank you. So Sheri, could you --

17 DR. FEHNEL: There we go. All right. Good
18 job. So again, like other people have said, I
19 think this is a really comprehensive, extremely
20 well written document. Obviously a lot of work
21 went into that. So thank you very much.

22 I think there's a theme, you know, in kind of

1 thinking about where we want to go and how we need
2 to get there.

3 And it seems like there's one thing about the
4 guidance that maybe is not completely clear, and
5 honestly, I didn't really understand until we had
6 a conversation kind of in preparation for this
7 panel, in that this document is really intended
8 for patients and patient advocacy groups, to
9 encourage research within these organizations.

10 It's hard for -- a lot of us have the hat on
11 of being used to either working in pharmaceutical
12 companies or working primarily for pharmaceutical
13 companies. There's so much in here about all
14 different sorts of research that might be done.

15 I think if we're thinking about the audience
16 and we're really thinking about organizations like
17 patient advocacy organizations, I think there's a
18 wealth of information there about that can be
19 gathered about the patient experience and maybe
20 not worrying too much about some of -- a lot of
21 the quantitative information that we've been
22 talking about and sort of trying to say that

1 everything needs to be generalizable and all of
2 that.

3 I don't think where we're going with this
4 guidance is going to end up being the final word
5 on almost anything related to drug development. I
6 think it's a beginning.

7 And so, I think this is a wonderful place to
8 start and I think maybe the focus really will be
9 more on qualitative research and really
10 understanding from these patient advocacy
11 organizations, you know, who have this wonderful
12 membership, a source of information, if we can
13 encourage some of these organizations to collect
14 some data on their own.

15 I've had the opportunity to work with a couple
16 of groups like that and I think by having those
17 folks collect some of these data themselves, it
18 may take out some of the bias that maybe comes in,
19 in the process of different pharmaceutical
20 companies or depending on how a drug works.

21 It's really focused on what is important to
22 this patient group. And I love that the FDA is

1 encouraging that kind of work. I think from the
2 perspective of the guidance, there's lots and lots
3 of information. And one thing that's really clear
4 is that there's lots of flexibility. And I
5 appreciate that as well. There's lots of
6 different ideas about how qualitative data can be
7 gathered.

8 One place that I didn't feel like there was
9 quite that flexibility is in the analysis of
10 qualitative data. In the appendix, it talks about
11 grounded theory specifically as FDA's
12 recommendation. And I think that was the only
13 place that I found a specific recommendation for
14 one method versus another.

15 And I think there, we have to think about,
16 well, what are we trying to do and make sure that
17 we have a qualitative analysis method that's also
18 fit for purpose, if you will.

19 There are also a couple of places in the
20 document that are talking about focus groups as a
21 place for cognitive debriefing. And personally, I
22 don't believe that that's really the right venue

1 for cognitive debriefing.

2 I feel like if you're really trying to
3 understand people's thought processes and how they
4 understand an item, how they're responding to it,
5 you really need to have that individual
6 interaction and really hear what that thought
7 process is rather than trying to have a group of -
8 - trying to have a group of patients do that or
9 feel like somebody's going to be willing to say,
10 hey, I don't understand what this question means.

11 You may not find that in a focus group. But
12 you're going to get that in an individual, in a
13 reaction. So I would think about maybe thinking
14 about that differently. But I think generally,
15 you know, there's so much information here.
16 There's a lot of good ideas.

17 You know, and I think that even the things
18 that, you know, maybe could be framed a different
19 way are really minor issues in the grand context
20 of things that I think could be easily addressed.
21 So, thank you.

22 DR. KOMO: Great. Thank you, Sheri. Gary?

1 DR. GLOBE: Thank you. I had the same
2 reaction as Sheri did. So I'm not sure what
3 patients could read and understand this guidance.
4 It's not for patients that I would -- I don't know
5 how they would really understand all these
6 methods.

7 I think it would be -- I'm not even sure the
8 advocacy groups would have people on staff that
9 could really understand most of this. It's good
10 information. But I'm just not sure how they could
11 use this and operationalize it per se.

12 What it would -- what I would think it would
13 tell them is you need to go hire people that can
14 then follow this for you.

15 And so, the other thing is that it doesn't
16 seem to really direct people down the most common
17 paths, the most common swim lanes that those of us
18 in industry need to follow to really have robust
19 data at the end of the day, whether it's for
20 regulatory decision or for label.

21 And I think that you can talk about Delphi
22 methods and other things. Those probably are not

1 the things that most people use. And so, I think
2 there's a lack of clarity about what's the most
3 common path that you're going to need to go down
4 to have something at the end of the day that could
5 actually go in a trial and be analyzed and be
6 presented.

7 And I think right now, you have an ocean of
8 opportunities, but nothing that's really saying
9 here's how it usually goes and here's what you
10 usually need to do. So those are my comments.

11 DR. KOMO: Great. Thank you. Isabelle?

12 MS. LOUSADA: So I think this is timely. I'm
13 a patient advocate. My organization is led by me,
14 a patient. And patient preferences, it's so
15 critical. Everything we do comes back to that and
16 should be the starting point. The model has to be
17 bedside to bench and back again. So this is
18 absolutely key.

19 And I think one of the things that we have to
20 think about, that how patients engage is -- we're
21 just sort of at the foothills of discovering the
22 pathway to doing this. I think we've seen with

1 the patient-focused drug development meetings,
2 which have been fascinating and insightful and we
3 have taken part in one, that they really -- there
4 are so many unexpected outcomes from them.

5 The other thing that we see is that for
6 organizations, for rare diseases and other
7 diseases, it's a huge amount of work to do one of
8 these meetings. And we're just capturing one
9 moment. And what we know is that we're capturing
10 a moment in a changing and evolving landscape.

11 So something that I think we need to consider
12 -- and I think it's wonderful to have engagement
13 with organizations.

14 But there are a number of things we need to
15 look at. One of them is that if an organization
16 like mine is investing a significant amount of
17 resources to do a study like this, what are we
18 asking. What is the outcome? And how do we
19 evolve as the disease evolves?

20 And the other bit that I think happens that is
21 it's easy to catch a patient preference at a
22 moment in time. But those change throughout their

1 journey. So how do we catch those? And it's very
2 different than getting a group of patients who
3 have advanced disease, different stages of
4 disease.

5 But actually tracking those changes because
6 those, in the end, are what really influences --
7 influence their decisions. It's where they are
8 and what's preceded their journey.

9 And likewise, as we capture this data from a
10 broad population, which we then choose the
11 pristine population for the clinical trial, we see
12 that in one of the diseases that I work with, they
13 have 1.5 comorbidities. They're on five
14 medications a day.

15 That's the population who will be taking the
16 medication. But they're not the ones that will be
17 in the clinical trial. So that's been
18 challenging. How do we take this data, that we're
19 going to collect the data.

20 Prospectively, we have ideas about the
21 questions we're asking. We need to make sure that
22 we have the rigor to interrogate the data to a

1 level that's satisfactory for the FDA. And
2 there's also pathways to then retrospectively be
3 able to go in and ask questions. So can we make
4 sure that we establish that in the beginning?

5 We need to then understand how that works in
6 with the trial and those endpoints, but also how
7 that data becomes used in the real world. So I
8 think there are a number of levels that it needs
9 to be looked at.

10 I think one of the things we need to
11 understand as patient organizations is what
12 partnership and guidance we can expect because, by
13 the very nature, you know, I sort of think I'm an
14 architect. And it took me 10 years to train and
15 five years in practice. And if somebody was given
16 a manual of how to design a building, it would
17 never have the nuances of the architecture.

18 And it won't have -- as organizations, as hard
19 as we might try, we will miss that, the nuances of
20 the science that you rely on. So we have to
21 understand what the flexibility is in this as we
22 collect and generate the data. And I think also

1 having some pathway to understand what the ability
2 of an organization is, so how do you rate what
3 you're able to do.

4 Our patient resources, our finances are
5 scarce. So we don't want these to be repeated in
6 many studies because we can't do that. So how do
7 we work through and identify when is the right
8 time to do one. What is the right thing to do?

9 At what point do we need to have external
10 support from experts, from the FDA, from other
11 organizations to really maximize the potential of
12 these hugely critical and important meetings?

13 So I could talk on and on about this. But I
14 want to just say I really think this is a
15 phenomenal effort. I think we just need to think
16 about this as we're looking at these guidance, you
17 know, coming through and for, it's such a circular
18 process.

19 And that fourth guidance will inform the first
20 steps that we do and, likewise, we need to think
21 of this very comprehensively, that it's not a
22 four-year plan, that how we can make sure that

1 this really is a continuing and evolving
2 conversation for each of these stages.

3 And I think just also talking through and
4 thinking about the flexibility that needs to be
5 considered and how more specifically we can engage
6 with FDA to make sure that the work that's being
7 done is a benefit. Thank you.

8 DR. KOMO: Great. I'd like to thank all our
9 panelists for all their thoughtful comments. At
10 this point, I think we'd like to address the --
11 let's see, where's the -- the questions to
12 address. So maybe if we could address the first
13 question.

14 So it's for future guidances, we'll discuss in
15 more detail qualitative, quantitative and mixed
16 methods in more detail or less. Is more detail or
17 less needed in the first guidance about which
18 source -- example, interviews, focus groups,
19 consensus panels, et cetera -- to use to collect
20 data?

21 Is anything missing? Include in your comments
22 feedback on the information in the appendices as

1 well. Would anyone like to start? Please, Steve?

2 DR. COHEN: Well, this is more related. I
3 think we've given a lot of attention to the
4 guidance in terms of those three areas.

5 But I was really intrigued by Isabelle's
6 comments in terms of how this really is also going
7 to be directed, a document for the patients.

8 And I was thinking in terms of what the
9 findings are, making sure the design has some sort
10 of a feedback loop to get it back to the patients,
11 and there is some sort of a portal where some of
12 the impacts from the study is made available to
13 them.

14 And having some sort of mechanism where in
15 many of the analyses, you're going to see results
16 gravitate towards the mean. But there are some
17 very vulnerable subsets of the population that
18 even if they're not really the core experience
19 that most of the individuals are having, they're
20 equally important.

21 And actually drilling down to those cases,
22 having the capacity to actually inform some

1 research or some interventions that could help
2 their lives I think would resonate well and sort
3 of -- so I was just thinking more about the
4 continuum of to get the information from the
5 patients, if you could make them front and center,
6 like in the driver's seat or like riding shotgun
7 in terms of it's a partnership. So I would just
8 put that perspective there.

9 DR. KOMO: Great. Thank you. Would anyone
10 else like to address this question? Isabelle,
11 please?

12 MS. LOUSADA: I was just going to say that I
13 think, you know, it's quite hard to separate
14 between the first and second guidance of what you
15 ask from whom.

16 But I also think the -- will help people to --
17 if there was more context and relation -- partly
18 in relation to drug development, to really
19 understand what the advantages are and
20 disadvantages are of different techniques to use.

21 So I think that would really help clarify and
22 at what times they might be appropriate to

1 consider each one.

2 DR. KOMO: Great.

3 DR. GLOBE: Yeah, in answer to that, so people
4 like me in organizations that develop products, we
5 see products coming up through the pipeline.
6 There isn't even always a lot of money in our
7 organizations for early products because nobody
8 knows whether they'll work or not.

9 And so, everyone's competing for funds. And
10 you tend to focus on the things that you think
11 will bring the most value, the concepts most
12 important.

13 So we tend to follow the PRO guidance. So
14 that's cardinal symptoms, proximate impacts. And
15 then, we don't even go further anymore now. We
16 don't even really think about quality of life too
17 much, which is sort of akin to what we're talking
18 about here today.

19 So it could take us two years and a million
20 dollars just to come up with those with a
21 proximate or a cardinal symptom measure. And
22 then, we might be barely ready by the time we get

1 to the Phase II.

2 And so, the question is what else could we
3 add, right? We already have a number of PROs. We
4 have a lot of items. What other concepts would we
5 bolt on? And how quickly could we get those?

6 And would we have really orchestrated that at
7 the right timing so that it could actually go into
8 a study, make it into the study? It's not -- it's
9 not going to be easy.

10 MS. LOUSADA: Yeah, and I'll just add when we
11 come to look at labels, as a patient, the list of
12 symptoms that you may have, the list of side
13 effects that may come out, having those all
14 listed, what patients really want to understand is
15 the nuances of those.

16 And so, while we understand that on the label
17 there isn't the real estate to do that, that's
18 really what we're getting at. And so, trying to
19 understand and tease that out becomes I think part
20 of what we have to look at and is truly
21 challenging and we have a long way to go on it.

22 DR. GLOBE: Sometimes the concepts that are

1 important to patients are not even going to change
2 within the period of time of a trial. So say a
3 person has certain coping mechanisms for their
4 disease, like in ulcerative colitis or Crohn's.

5 Some of those coping behaviors won't change
6 until way after the trial. So you could try to
7 measure that very important concept to the
8 patient. But it's not going to change in the
9 trial.

10 So you also have to make sure that you're
11 measuring things that are going to happen during
12 that 24-week period or 48-week period. And they
13 may not always be the things that are most
14 important to patients.

15 DR. FEHNEL: I think for me this kind of goes
16 back to sort of what's the overall goal of the
17 guidance. I don't think it's is meant to be
18 complementary or supplementary to the PRO guidance
19 where we're talking about, you know, developing
20 COAs.

21 I think if we get too focused on that, we may
22 miss some things that are really important and

1 some opportunities to gather data from these
2 patient advocacy organizations. We keep going to
3 these -- you know, even in a lot of what we're
4 doing right now is in rare diseases.

5 And there was a comment made earlier, kind of
6 that Laura Lee made, about data reuse. And maybe,
7 you know, there's some discussion in the guidance
8 document about limiting patient burden. And I
9 immediately went, oh yeah, we're not going to ask
10 everything every day.

11 But we're also burdening patients and KOLs and
12 these advocacy organizations because we're --
13 people like me are coming to them, you know, on
14 behalf of multiple different pharmaceutical
15 companies working in the same area. And we're
16 often asking about the same sorts of things of the
17 same people and demanding, you know, their time
18 and resources.

19 And if there was some way to really encourage
20 more of these advocacy organizations to do some of
21 their own research, and I recognize that funding
22 needs to happen to be able to do that. But we're

1 working with one organization now that's
2 developing a registry. And their idea is that
3 eventually that will actually produce funding by
4 helping pharmaceutical companies recruit patients
5 for their clinical trials. So there's sort of a
6 business model kind of in there.

7 But what they're going to have is this
8 incredibly rich source of data about what the
9 patient experience is and who these patients are.

10 And I think having it encouraging some of
11 these organizations who basically nobody cares
12 more about these patients than these
13 organizations, to be able to fund some of that
14 work or to work collaboratively with these
15 organizations, I think we could have a wealth of
16 information about the patient experience.

17 And then, maybe the PRO instrument
18 development, that kind of comes later. Like this
19 -- I think this is just a beginning to that
20 process. I don't think it's the end. And maybe
21 I'm misunderstanding. But it just seems like
22 we're going too far.

1 DR. GLOBE: You know, it was my -- maybe I
2 misread, but it was my understanding that
3 Isabelle's going to have to generate items that
4 are going to go into our trial.

5 DR. FEHNEL: I hope not.

6 DR. GLOBE: That -- yeah, because otherwise,
7 we can't measure it longitudinally and see if
8 anything changed.

9 DR. JOHNSON: So I'm going to jump in here,
10 Scott. Sorry to take that prerogative away from
11 you. But I do think that we see this work as
12 being complementary to the PRO guidance.

13 So just to be clear, much of this came from --
14 you know, the PRO guidance, for those of you all
15 who don't know, was finalized December of 2009.
16 So it's been about eight years, almost to the day
17 now. And Elektra can talk more about that because
18 she was here when that was all happening.

19 But one part of how these guidances came into
20 being was our looking back and saying, okay, this
21 guidance has been out there. And what are some of
22 the issues we're still having? And also, what are

1 we hearing from patient advocacy groups, that
2 we're hearing from sponsors, that we're hearing
3 from some of these expert groups that are hired
4 and what pushback are they getting internally as
5 to what needs to be done?

6 So Gary, I think you talked about this a
7 little bit. But I do want to say that our hope is
8 that the patient groups do hire experts.

9 So it's not that necessarily individuals are
10 going to go out and do all this work on their own,
11 but that they are informed consumers about the
12 wares that are coming out because we realize, you
13 know, there is limited time which may be the most
14 precious commodity that everybody has and limited
15 money, which is also very precious and true.
16 That's an issue for everybody involved.

17 But when we give exact swim lanes, that tends
18 to be all we see. And so, we want to make sure
19 there's flexibility because we will then hear back
20 sometimes, now okay, if you give not even the
21 parameters of the pool, then there's a problem
22 too.

1 But one time, you know, we hear -- not just
2 one time, many times -- an expert will say, okay,
3 this is what's needed or a patient group wants to
4 do something. But there's an underestimate on
5 behalf of the people with that money as to what
6 actually needs to be done.

7 So part of what we're hoping to put forward is
8 kind of scoping this is what may need to be done.
9 If this is your goal, here are the things that you
10 need to consider.

11 And if you're not going to be able to consider
12 each of these, you might need a different goal or
13 other partnerships or other ways to work together.

14 So this is -- again, it's complementary,
15 trying to fill in some of the issues that we've
16 been seeing as regulators with what has come to us
17 but also being forward-thinking, because the world
18 may have been at a very different place in all of
19 those early 2000 discussions that led to that 2009
20 guidance.

21 I don't know if Selena, Elektra or others have
22 something they want to add to that?

1 DR. PAPADOPOULOS: I'm going to be very brief
2 because I really want to hear from you all. But I
3 think that, you know, this is much broader than
4 just the COA.

5 I think, you know, if a patient group is going
6 to put together a meeting and they're going to try
7 to map out the patient journey, being forward-
8 thinking and trying to think ahead, okay, what can
9 this information be used for.

10 Can it be used not only for the COA
11 development and the endpoint development, but
12 understanding who to enroll in studies, what the
13 eligibility should be, understanding, you know,
14 what are the unmet needs of patients,
15 understanding things like what do they value, what
16 are their preferences, what risk and uncertainty
17 they want to take.

18 So this is very far upstream from the actual
19 endpoint. Yes, it will be used to inform the
20 actual endpoint. But to me, it's much broader
21 than that and I don't think we should focus
22 prematurely on just the COA.

1 DR. DANIELS: Yeah, so I'll echo the comments
2 that Laura Lee and Elektra just said. But I want
3 to try to redirect us back to this question in
4 terms of methods.

5 Are there any methods that you think that we
6 may be missing in this discussion document,
7 anything that you guys can think of?

8 DR. FEHNEL: Really for me, just the issue of
9 the qualitative data analysis and, you know, just
10 making that as flexible as everything else in the
11 document, which is great.

12 DR. KOMO: Okay.

13 DR. PAPADOPOULOS: Maybe -- maybe one other
14 question is, you know, rather than are there any
15 methods missing, are there any methods that maybe
16 should be emphasized a little bit more so that
17 we're not losing, you know, the forest for the
18 trees?

19 DR. RUGGERI: Could I give a slightly annoying
20 response to that, by sidestepping it but trying to
21 answer it at the same time? With the work that we
22 do, we're often provided data long after the

1 original collection and asked to try to make sense
2 of it with a very broad question.

3 And one of the things we find is that it would
4 have actually benefited those who are collecting
5 it originally to understand what useful data looks
6 like, more so than understanding how we analyze
7 it.

8 And for those who are generating it and may
9 not later be responsible for analyzing it in a way
10 that gets used in policy or in regulation, to
11 spend more time emphasizing what does good, clean,
12 reliable data look like, how does it get generated
13 and how do we get a nice sample of people, whether
14 it's representative or not, engaged in that
15 material so we can rely on what they're providing.

16 Non-representative samples are something that
17 can be worked with if the data is easy to work
18 with. You can have a great representation and
19 really well-done sampling of really bad data
20 that's incomplete.

21 And I think the emphasis really could focus on
22 what does it mean to generate something that

1 others can use or that the people generating it
2 can use. That's really where the investment I
3 think can be made all the time because you can
4 always get support. There's plenty of reference
5 material. You know, the supercomputer -- or
6 sorry, statistical computing has gone, you know,
7 exponentially in the last 10 years in terms of who
8 can make use of it.

9 So I think the best methods really focus on
10 how to generate good data, not trying to
11 comprehensively cover every possible analytical
12 approach because in some cases I'm actually
13 getting more and more concerned how much
14 analytical methods have been overly simplified and
15 people are throwing them into statistical
16 algorithms.

17 I know a lot of people that do machine
18 learning that never understood fundamental
19 statistical principles. And I think in that case,
20 it's more important to emphasize and invest in
21 really that methodological understanding of how
22 data get generated. So I hope that's a reasonably

1 useful.

2 DR. KOMO: Steve, I had a question for you.
3 So you had mentioned in your initial that a
4 variety of analytical approaches and is your
5 thought that that should be included in the
6 document?

7 DR. COHEN: -- the analytical question, the
8 most appropriate analytical technique. But I
9 guess I was gravitating towards more -- as you
10 were mentioning the data going into this effort,
11 again, it's primarily on patient experience data.
12 But any design that also facilitates linkage, I
13 think electronic health records was brought up,
14 physician medical records, claims data.

15 That's the gift that not only gives pre-
16 dispositional information but gives ongoing
17 continuous longitudinal connectivity and outcomes
18 over time to the extent the patients allow for
19 that and, on the other side, whether it's the
20 provider or it's the insurance carrier would make
21 that data available.

22 But that's something to the extent, right at

1 the get-go, you could built in this data
2 integration mechanism that would give more power
3 to the underlying research questions, how -- what
4 the patient experience is, many times there's an
5 asymmetry in terms of they might really enjoy, you
6 know, the connectivity of the protocol they're
7 getting.

8 But it's not really doing any good for them or
9 something like that. So you know, understanding
10 those nuances when you're planning your study.
11 But again, I'd push on designs that would try to
12 bring some coverage to integrated designs.

13 DR. KOMO: Thank you. Anyone else?

14 DR. GLOBE: Can I make a -- I think this is an
15 increasingly important topic because very soon,
16 especially with the way social media has driven
17 this, qualitative data is soon to be, if not
18 already, analyzed in the same way we analyze
19 quantitative data because the statistical
20 computing power is there now.

21 And I think those linkages are going to be
22 incredibly important to understand alongside

1 because if we understand how to link different
2 sources together, then that really massively
3 increases the value of every data set, even if it
4 wasn't initially intended to be used in the same
5 set of analyses or body of work.

6 DR. KOMO: Anyone else want to address this or
7 talk about this question before going to the next
8 one? Okay. Great. All right.

9 So the next question would be -- that we'll
10 address is a similar question about
11 operationalizing and incentivizing data collection
12 and also data management. So please go, Steve.

13 DR. COHEN: Just being tied to a lot of data
14 collection efforts where it's not just the front
15 end, but it's all the outputs and the analysis,
16 tremendous amount of attention is given to the
17 backend quality control of the data coming in.

18 And to the extent in data management, right at
19 the front, understanding the design, building in
20 the quality control checks, fixes to the data, to
21 the extent there is a computer-assisted interview
22 mechanism, if some response is either

1 inconsistent, having those corrections or bringing
2 it to the attention of the patient will really
3 minimize all the efforts post-data collection to
4 cleaning the data.

5 And you know, the capacity to do that is
6 available for those that are using computer-
7 assisted techniques. So to the extent one can
8 capitalize on that, there'll be a lot of
9 efficiencies down at the end when the data comes
10 back.

11 MS. LOUSADA: So I would just add I think that
12 it was very well-covered in the guidance. And the
13 only part I thought was missing is that it would
14 be helpful to understand the limitations of the
15 different approaches.

16 DR. KOMO: Okay. Great. Thank you.

17 DR. RUGGERI: I would only go back briefly to
18 a point I made earlier about biases.
19 Operationalizing your standards are excellent and
20 very helpful in research, as long as we haven't
21 biased those standards that we set that drives the
22 narrative we're already trying to drive, and an

1 example being if you're doing research in mental
2 health, what's the threshold for someone having
3 depression or not.

4 That could be looked at very differently
5 depending on the narrative that's trying to be
6 used and the state of the research.

7 So I think as long as those biases are checked
8 as things are operationalized and standard and
9 people who are setting those for themselves are
10 aware of that, I think then this has done a very
11 good job. I just think that could maybe be raised
12 to the forefront a little bit.

13 DR. KOMO: Great. Thank you. How about maybe
14 we can move on to the next question now, whether
15 there are any other factors to consider regarding
16 the selection methods to collect, analyze patient
17 experience data that should be included in the
18 guidance? I think we sort of addressed that, but
19 --

20 DR. FEHNEL: So in collecting qualitative
21 data, there were a number of different modes that
22 were sort of offered as potential. And they sort

1 of focus on being able to have good quality data
2 and representativeness of the data.

3 The only thing I would also encourage is that
4 thinking about kind of patient comfort and being
5 able to build a rapport. I think a lot of times,
6 there's really no substitute for in-person data
7 collection with qualitative research.

8 I think particularly some of these patient
9 populations, you know, we do so much in rare
10 disease and folks want people to understand, you
11 know, what they've been through. And I think you
12 can collect a lot of data through the Web and
13 through phone and that sort of thing.

14 But I just find that the richness of the data
15 that we capture when we're sitting in a room with
16 somebody and we can really observe their body
17 language and really listen to their stories and be
18 present with them, that to me there just isn't a
19 substitute for that. I feel like I understand it
20 better when I've spent time with somebody.

21 DR. KOMO: Thank you.

22 MS. LOUSADA: And I would just add to that we

1 have, one of our populations, very sick. The
2 treatment is very difficult. And the choice about
3 survival versus treatment is a really challenging
4 one and it's something that should be addressed.

5 Who is able to elicit that information and who
6 should has to be very carefully thought about and
7 how that's -- how those patients are handled and
8 curated because otherwise you will not get
9 accurate representation of their feeling.

10 And the other part I would just add is I think
11 it would be very helpful to contextualize and give
12 some examples where possibly it goes through and
13 embeds in the -- from early development through to
14 early stage drug development and sort of early
15 understanding about which tools, giving some
16 examples of which tools might be good ones to
17 consider or examples of that would be helpful.

18 DR. KOMO: Great. Thank you. Yes?

19 DR. COHEN: Just one more thing in
20 capitalizing on the qualitative. Either right at
21 the beginning of the survey or clearly at the end,
22 informing the respondent, the patient that if

1 there was anything missing from this survey that
2 really impacted on what was being studied, there
3 should be a mechanism to capture that. And
4 perhaps right at the -- that would be at the end.

5 But at the front, bring that to their
6 attention, that if there were any questions that
7 they were struggling with, there should be a
8 mechanism to bring either an uncertainty of
9 response to the data that was coming in and in the
10 analysis profile.

11 DR. KOMO: Great. Thank you.

12 DR. GLOBE: I would just add one more thing.

13 DR. KOMO: Sure.

14 DR. GLOBE: Just it's hard, even when you're
15 trying to develop a cardinal symptom or a
16 proximate impact measure, to get very severe
17 patients. That's usually the most challenging
18 group to recruit and, you know, it's very
19 important to hear them.

20 So, you know, it would be great if we could
21 come up with some other strategies for how to
22 actually get their voices into this development

1 work. Usually if you have 40 patients, you know,
2 just a couple of them are very severe because they
3 can't come in and be interviewed or they don't
4 want to participate.

5 So I think that might be a place where you
6 could work with, you know, other groups and maybe
7 we could use some hybrid strategies to get their
8 voice included in that work.

9 DR. KOMO: Have you found that does that work
10 better than others that you might be able to
11 suggest?

12 DR. GLOBE: I'm sorry?

13 DR. KOMO: Have you found that there's a --
14 did it work best to get the very severe patients
15 in?

16 DR. GLOBE: Well, it goes back to
17 representativeness. Usually that's a -- we do
18 want to get some sampling of it. But it's usually
19 always barely enough or it's a small amount
20 because it's just very hard to get those sickest
21 of sick patients to want to participate.

22 So if there were other ways of us doing that

1 and getting that input in some way, that would --
2 that could be helpful.

3 DR. KOMO: Theresa?

4 DR. MULLIN: Oh no, I think that I would just
5 say to Gary, I think we've got examples of how
6 that could be possibly handled in the discussion
7 document. But I guess we'd invite your views to
8 see if you feel that that's enough.

9 I think we talk about a basic approach, maybe
10 a focus group or some approach like that. And
11 maybe using another method to augment the group
12 that you've got included that way to get at some
13 of those other subpopulations.

14 But please look at what's there to see if you
15 think it addresses this issue. Thank you.

16 DR. KOMO: Thank you. At this point, I'll
17 open the -- does this panel have any more comments
18 before I open to the floor? Okay. Great. Does
19 anyone in the audience have questions?

20 AUDIENCE QUESTION AND ANSWER

21 MR. BARTEK: Hello. I'm Ron Bartek. I'm a
22 patient advocate, president and cofounder of the

1 Friedreich's Ataxia Research Alliance.

2 I'd like to first thank the FDA for convening
3 this meeting and thank them moreover for creating
4 and driving patient-focused drug development from
5 well before it was congressionally mandated and
6 doing such a great job with that.

7 I'd like to then voice what I think is sort of
8 an underlying frustration that a lot of us are
9 feeling because of the confusion between possible
10 measures or tools that would report on the -- how
11 we can better understand and characterize our
12 diseases, you know, conducting surveys and things
13 that will help instruct that understanding and
14 characterization and even populate our natural
15 history studies and so forth, confusion between
16 that kind of measure and tool and the kind of
17 measure and tool that was raised in the very first
18 comment this morning about measures and tools we
19 can use to report in clinical trials.

20 And that's so important to a lot of us in the
21 room now because we're getting strong
22 encouragement from our review divisions saying,

1 okay, you've got your primarily endpoints that
2 you've developed over the years, you know, from
3 your natural history studies and so forth. That's
4 wonderful.

5 But as long as we keep hearing, you know,
6 signals of improvement or signals or benefit, that
7 can or may or may not really report on the way the
8 patient is feeling and functioning and surviving,
9 we need additional evidence.

10 We need additional evidence demonstrating that
11 the patient is feeling and functioning better, to
12 at least the same extent that you're reporting in
13 these signals from your primary endpoints.

14 What they're really saying is give us another
15 reason to say yes. And you know, so what we're
16 all struggling to figure out is how to collect
17 that additional evidence in the midst of a
18 clinical trial where we're getting an incremental
19 -- a signal of incremental improvement from our
20 primary and even secondary endpoints.

21 And our reviewers are saying give us evidence
22 that the patient is feeling and functioning better

1 to at least that same extent.

2 So maybe as you're drafting the guidances, you
3 might want to differentiate between measures that
4 are helping with surveys, tools that are helping
5 you collect information from your patients as to
6 how to characterize which symptoms are important
7 to them and so forth and how to populate your
8 natural history and measures and tools that you
9 can use in clinical trials to report and to
10 measure and report compellingly and reproducibly
11 the way the patient is feeling and functioning in
12 the midst of that clinical trial to add to your
13 primary endpoints. So just a --

14 DR. KOMO: Thank you.

15 MS. KENNEDY: Hi. Good afternoon. I'm Annie
16 Kennedy, with Parent Project Muscular Dystrophy.
17 And I just want to start with a thank you to all
18 of you for being here and for helping us get here.

19 Today is really I think a landmark day for
20 many of us in the community. Many of us in this
21 room worked very hard on the 21st Century Cures
22 legislation, along with many of you and spent many

1 years working on the provisions in that
2 legislation.

3 And so, we're very excited to see the
4 discussion draft come out that really reflected
5 the spirit of those discussions that took place
6 over the years that led up to the passage of that
7 bill and then to the guidances that are now coming
8 out.

9 To that end, I just wanted to maybe go back to
10 the clarification that Laura Lee did, which I
11 think was incredibly important, and thank you.

12 And that one of the things that went into that
13 provision that we're here to discuss today was
14 that we were really looking to ensure that there
15 were signals back to all of us who were innovating
16 in these spaces, that this wasn't a trend, that
17 the science of patient input is really here to
18 stay and is incredibly important to FDA.

19 And those of us who've been here engaging with
20 you know that and feel it and believe it. But
21 especially the patient groups who are investing in
22 it, the industry groups that are investing in it,

1 needed -- we talk about signals. And I've heard
2 Theresa say many times what signals do you need.
3 And this discussion draft, this guidance is one of
4 those signals that are needed.

5 But it wasn't -- the intention wasn't to shift
6 the responsibility to patient groups to be doing
7 all of the work. It was to make sure that
8 industry also continues to invest.

9 And many of the people in this room are those
10 in industry who do the job and do the functions,
11 but needed to understand how it's being used in
12 regulatory decision-making, how to continue to use
13 our data that we're producing, that they're
14 producing from patient communities within their
15 protocols, et cetera.

16 So if you could just clarify that this
17 guidance isn't being written just for patient
18 groups, but it is being written for all of those
19 stakeholders who are listed in Title II,
20 Subsection A, that all of the groups who are
21 working in this space are the intended recipients
22 of the guidance, that would be incredibly

1 important.

2 DR. JOHNSON: Yes.

3 MS. KENNEDY: Thank you. And then, the second
4 part of that is that, to the comments that were
5 made today around that this might be a little too
6 in the weeds for patient groups, I would argue
7 that it's not too in the weeds for a lot of
8 patient groups.

9 So a lot of patient groups, we are hiring
10 capacities, we are hiring people who do these
11 jobs. We're contracting with people who do these
12 jobs. Or in the comment that was submitted by the
13 patient advocate who wasn't here earlier today I
14 think really framed it nicely.

15 We're working on precompetitive partnerships
16 very early on with our industry partners, with
17 social scientists so that we're ensuring that the
18 right people are at the table with us when we get
19 started.

20 And so, the guidance that you're developing
21 around the methodologies, around the taxonomy is
22 incredibly important to us to make sure that we're

1 creating data that you need, that you can use and
2 that's informing the decisions that you need to
3 make. So, thank you.

4 DR. KOMO: Thanks. Please?

5 MR MOEHRING: Good afternoon. My name is
6 Henry Moehring. I'm with the Alpha-1 Foundation.
7 And I'm Alpha-1 patient myself. I could not have
8 said it better than my two colleagues earlier and
9 my initial reaction was to go sit down. But I
10 want to emphasize those points.

11 The document is appreciated. We thank you for
12 the work that has gone into it. We are committed
13 to the project as well. In our community, we have
14 a very strong patient voice and that voice wants
15 to be heard. And I think we're looking for ways
16 to effectively support that process.

17 I've walked away with some things today. But
18 the message is strong that we can't do this as a
19 patient community alone. And we are dependent on
20 the bigger partnership. The voice or the
21 expertise that I have is the expertise that I have
22 as a patient. I'm not a statistician. I

1 appreciate your analogy to an architect. I'm the
2 MBA guy. When you get to the point about writing
3 the budget, call me because I'm really good at
4 that.

5 But the statistics part is not where we're at.
6 But we bring that information to the table that I
7 think can make a difference and finding a solid
8 voice to carry that forward is something we're
9 committed to.

10 The last point I would make is we also are
11 looking at longitudinal studies and longitudinal
12 information gathering sources. And I hate to use
13 the term registry because it seems to pigeonhole
14 it. This document would seem to support those
15 efforts as well.

16 And as a patient, I understand the process
17 going out to 2020. But as a patient, that's a
18 very long time. So the sooner that information
19 can flow so that we can formulate our questions
20 today to have better answers for you when we sit
21 with sponsors. So thank you very much.

22 DR. KOMO: Thank you. At this point, I'd like

1 to give our panelists, they have one thought
2 before we wrap up? Anybody? Does anyone have
3 anything else they'd like to say?

4 Okay. Well, I'd like to thank everyone for a
5 very informative and your thoughtful comments.
6 We've heard quite a bit in this session. Let's
7 see.

8 So I think some things we heard were -- some
9 takeaways were -- you know, that some of it is --
10 while generally we want to have more details that
11 are refined, sometimes we want to highlight the
12 principles that are critical so we don't get sort
13 of overwhelmed with the details.

14 There was a large we always do want to worry
15 about bias from both the quantitative as well as
16 the qualitative sides of it. And I think we want
17 to make sure that analytical strategy should also
18 be looked to and used, the early results to help
19 inform the later studies.

20 And the reproducibility is critical. And
21 also, sort of with the -- what we need to always
22 think about and be mindful of is now with the link

1 -- possibility to link the linkages that
2 potentially that ensure that the data is not
3 identifiable. There were some suggestions to add
4 more references.

5 I think it's very clear that we need to be --
6 we want to encourage the patient advocacy
7 organizations that collect the data and recommend
8 more flexibility in the qualitative analyses.

9 I think also we want to -- so there was some
10 discussion -- we had some discussions on how best
11 to do this with some of the rare diseases, which
12 was very helpful.

13 And I think what's critical, I think what's
14 important is this is that we want so not just
15 patient advocacy groups but also the -- all the
16 stakeholders will be working in this space. So we
17 want to encourage that. So thank you very much.

18 (Applause.)

19 MS. VAIDYA: Thank you, Scott. And thank you
20 to our panelists for a great discussion. Now, I'd
21 like to invite our session three panelists and
22 Sara Eggers from the Office of Strategic Programs

1 in CDER will be moderating this session with Megan
2 Moncur. Yeah, Megan Moncur. So --

3 SESSION III: TRANSLATING BEST PRACTICE INTO REAL
4 PRACTICE - DEVELOPING GUIDING EXAMPLES

5 DR. EGGERS: Good afternoon, everyone. I'm
6 Sara Eggers. I'm from the Office of Strategic
7 Programs. And while we get set up here, I'm going
8 to invite you to stretch your toes. I know those
9 are the most comfortable chairs that we have on
10 FDA's campus. That's why I chose to sit up front
11 in this more comfortable chair up here.

12 So get up, stretch your toes, shake your legs
13 out and we'll just get everyone setup up here. It
14 can have a laugh too. I know it always makes for
15 a laugh when you have to get up.

16 All right. I think we have everyone up here
17 and ready to go. We have learned a lot today and
18 our heads are spinning. But this is the fun part
19 of the day where we try to make it real. We've
20 heard a lot this morning and this afternoon about
21 the methodological issues and the practical
22 implications. And we also recognize that any

1 guidance, eventual guidance that comes out needs
2 to help translate the best practice into real
3 practice. And we hope to do that through guiding
4 examples.

5 And so, the focus of our session today, in a
6 nutshell, is to discuss what would make examples
7 be really good examples of the stakeholders that
8 are the target of this eventual guidance document.
9 Some examples are embedded in the document. Some
10 examples are embedded in the document.

11 For example, defining the research objective
12 for HIV or discussion about mixed methods research
13 in diabetes. These are peppered through the
14 discussion document. And we want to get some
15 feedback on those today.

16 But we also think there may be a bigger
17 opportunity to expound on some of the things that
18 we've talked about today that can get into a
19 little bit more detail through vignettes or
20 scenarios that could be appended to or somehow
21 otherwise linked to the eventual guidance.

22 And that's what we want to discuss today.

1 What a good one would look like, what features it
2 would have and what things should we highlight
3 through examples and through a big longer
4 treatment scenarios.

5 So we have a great set of panelists today. I
6 find that it's best for panelists to introduce
7 themselves. So I'm going to ask you all just to
8 go down the line and just say who you are and
9 where you're from. And we'll start with April.

10 DR. NAEGELI: Good afternoon. April Naegeli,
11 senior research scientist at Eli Lilly and
12 Company.

13 DR. MCCUNE: Good afternoon. Susie McCune.
14 I'm the director for the Office of Pediatric
15 Therapeutics in the Office of the Commissioner
16 here at the FDA.

17 DR. GERSHON: Richard Gershon, vice chair for
18 research at Department of Medical Social Sciences
19 at Northwestern University.

20 DR. IRONY: Hi. I'm Telba Irony. I'm from
21 the Center for Biologics. I'm deputy director of
22 the Office of Biostatistics and Epidemiology.

1 MS. OKUN: Hi. Good afternoon. I'm Sally
2 Okun. I'm the vice president for policy and
3 ethics at PatientsLikeMe and I'm also the human
4 protections administrator.

5 DR. STUART: Hi. I'm Liz Stuart. I'm
6 associate dean for education and professor -- I'm
7 a statistician by training -- at Johns Hopkins
8 Bloomberg School of Public Health.

9 DR. EGGERS: Great. Thank you, Liz. All
10 right. So we have, in the same style we've done
11 our other panel sessions today, we're going to
12 invite our panelists up here to give a few minutes
13 of remarks.

14 They've reflected on the overall objectives
15 that we've put forth about really maximizing this
16 translation into real practice through examples
17 and the questions that we have put forth here to
18 them.

19 And then, we will discuss today a couple of
20 things. We have some FDA colleagues up here who
21 are not -- have not been as part of the -- are as
22 intimately involved in this discussion document

1 draft. So you are also being asked to think of
2 examples where things might not have gone as
3 planned or where there are challenges or where
4 there are novel opportunities to illustrate
5 through examples.

6 Also, we're not intending to rehash
7 methodological considerations up here. It's
8 really just how we're going to take what we've
9 discussed already throughout the day, a lot of
10 which I think is very relevant and will come up
11 again through our discussion of examples.

12 So I'm going to start with April. If you
13 could just give a few minutes of responses?

14 MODERATED PANEL DISCUSSION

15 DR. NAEGELI: Sure. Great. First, thank you
16 for the opportunity to be a part of this panel
17 today. I commend, as everyone else in the room
18 today, FDA on this discussion document.

19 It's apparent that it was well thought out and
20 a lot of input has gone into that. So given the
21 breath of the audience and the stakeholders that
22 are targeted for the guidance documents, it is

1 important to acknowledge that a lot of tremendous
2 amount of preparation goes into planning and
3 conducting a study to collect patient experience
4 data and also too that, you know, each study that
5 is done is valuable in itself.

6 And it will take more than just one study in
7 order to meet, in the end, the evidentiary
8 standards that are required in drug development to
9 meet FDA expectations.

10 So the examples in the discussion document
11 seem appropriate in my mind and reflective of the
12 research that may be initiated by any of the
13 stakeholders to collect patient experience data.

14 The examples are high level. And I think as
15 was mentioned in the previous panel discussion,
16 perhaps consider putting the examples more in the
17 context for the intended use in the medical
18 development program process as well as how is it
19 going to be used in regulatory decision-making.
20 So thinking about how it could be used and for
21 these purposes.

22 Full case study examples would be great.

1 Having an example that could then -- components of
2 it could be pulled to each of the various sections
3 to put things into context would be -- would be
4 nice and also having examples on common diseases,
5 common diseases with comorbidities, as we heard
6 this morning from the diabetes examples and also,
7 as we've been hearing, rare diseases it's
8 important to help us understand.

9 So how does this research fit into the
10 benefit-risk framework and, in the end, clinical
11 trial design and endpoints?

12 A few concepts that I think are important to
13 further expand on examples are identifying the
14 target patient population and dealing with the
15 heterogeneity that you see in target populations.
16 Ultimately, clinical trials focus on specific
17 populations that may be subgroups where the
18 highest unmet needs are.

19 So making sure that the data is available and
20 able to go back and analyze to look specifically
21 at these important groups that where the unmet
22 need may be focused.

1 Additionally, recall bias, it should be
2 acknowledged that it occurs. We heard in the last
3 panel that patients -- you know, the most severe
4 patients aren't always participating in our
5 patient experience research because they're very
6 sick.

7 So patients will be on medication. And so, we
8 will have to ask them how did you feel, how did
9 that impact you. So just acknowledging that
10 recall bias is a factor and note it as a
11 limitation. So I'll stop there.

12 DR. EGGERS: Thank you so much, April. We'll
13 go to Susan.

14 DR. MCCUNE: Thank you very much. I want to
15 thank the organizers for inviting me today. I
16 think I'm the voice of pediatrics maybe here
17 today, which is really exciting.

18 But I am not clearly the only one because
19 other folks have brought up the pediatric arena.
20 And I'm thankful for the example, the pediatric
21 example that is already in the document.

22 I would say that I think it's really important

1 to remember both the patient and the parent or
2 caregiver viewpoint, especially in terms of the
3 impact on their lives. We think about pediatric
4 patients as potentially not being able to give as
5 much information about their disease.

6 But I think you have to recognize that
7 children who have been in the medical health
8 system from a very young age are really able, even
9 at a very young age, to talk about the impact of
10 their disease on their lives.

11 And so, it's critically important to be open
12 to collecting data from all of these patients,
13 even the youngest patients. And also, recognize
14 that the patients and their parents may actually
15 have a different outlook on their disease and
16 trying to capture those differences.

17 I think it's important to understand that one
18 method to be able to capture information from a
19 parent or a caregiver may be very different from
20 the type of tool that you would use to collect
21 that data from a young child and then from even an
22 older child.

1 I also wanted to talk about the fact that we
2 were talking a little bit about consortia and
3 collaboration in this last session.

4 But I think it's critically important to
5 leverage the work of consortia efforts in this
6 collaborative space in order to decrease the
7 burden that we were talking about and also have
8 increased access to patients, caregivers and
9 clinicians.

10 And two examples of this, one is the
11 International Neonatal Consortia, where they're
12 bringing together stakeholders from academia,
13 industry, patient/parent advocacy groups and
14 regulators all to discuss neonatal-specific
15 diseases in the precompetitive space and how to
16 approach those.

17 That might be a nice opportunity, these kind
18 of consortia efforts, to be able to bring these
19 groups together.

20 I'd also mention in the pediatric space
21 there's the International Children's Advisory
22 Network, or ICAN, which is actually a group of

1 children of various ages that have been asked to
2 provide input on clinical trials. And so, these
3 are all mechanisms by which we can actually expand
4 access to patients with particular diseases.

5 I will also -- I just wanted to say that we
6 have a couple of other groups that are
7 facilitating access to pediatrics through
8 pediatric trial networks.

9 One of them is Duke for the Duke Clinical
10 Research Institute and the other is the Institute
11 for Advanced Clinical Trials for Children. Both
12 are working to develop clinical trial networks in
13 pediatrics and would be an opportunity to be able
14 to access patients, parents and clinicians.

15 And I also wanted to just point out that there
16 may be some gaps in groups that are willing to
17 provide information in terms of their disease.

18 But then -- and that includes patients,
19 parents and physicians. But then, they're not
20 willing to then participate in clinical trials or
21 have their patients participate in clinical
22 trials.

1 So I think that there's a gap there that as we
2 are able to obtain more information about where
3 the needs are from a patient/parent/physician
4 perspective, that we also have to look at what
5 some of those reasons are for why they either may
6 not want to participate in the data collection
7 about their disease or the risk-benefit associated
8 with that. And then, why they might not want to
9 participate in clinical trials.

10 And then, just finally, I wanted to talk one
11 second about recognizing international trials
12 because in the pediatric arena we're doing a lot
13 in terms of international trials and making sure
14 that the tools are understandable for folks
15 globally but also understanding that, depending on
16 where you are in the world, the risk-benefit
17 associated with your disease, both for pediatric
18 patients and for their parents, might be different
19 and recognizing that.

20 And then, finally, we talk a lot about
21 multiple technologies that we're able to access in
22 order to be able to generate this information.

1 And I will tell you that for someone my age, I'm
2 talking about doing things with these things is a
3 little daunting.

4 I will tell you that for the adolescent
5 population and even for the younger pediatric
6 population, they are all over these kinds of
7 technologies.

8 So having the parent or the caregiver or the
9 physician using certain tools may be very
10 different from what would be the best tools to use
11 in the pediatric population. So, thank you.

12 DR. EGGERS: Thank you so much, Susan. And
13 Richard?

14 DR. GERSHON: Really, I had a hard time with
15 the examples because first I thought these are
16 great. And then, I thought, oh, there are little
17 problems here. And then I thought I'm not sure I
18 can improve on them. So, but I'd first like to
19 echo, I think, Theresa, your earlier statement.
20 These are merely examples.

21 And actually, I'd like to see the document
22 changed even to highlight that more firmly. I

1 think there's a historical, maybe it's just human
2 nature to say an example or the way we did things
3 yesterday are more likely to lead to a drug
4 approval or to FDA approval. And I think that
5 would be a mistake.

6 And because of that, you know, enabling a
7 process to preapprove novel methods, perhaps in
8 advance of a clinical trial to help facilitate
9 continued growth, while minimizing the risk to
10 study sponsors, who I think otherwise are going to
11 stick with the old things because we know you are
12 going to improve them and perhaps outdated
13 research methods.

14 And as we just talked about, phones and things
15 like that, these are -- we're going to be -- we're
16 going to be living in a bleeding edge
17 technologically speaking for the rest of all of
18 our lives. And it's going to be extremely
19 difficult to ever have enough examples that keep
20 current with that.

21 And I just want to be picky about a couple of
22 the examples to show ways where they could be

1 misinterpreted or misused. And again, I always
2 say, well, if you've got a problem with it, make
3 it better. I'm not sure I can. So, but it's just
4 maybe perhaps an issue of pointing out to people
5 they're exemplars and they could have issues too.
6 You have to think them through.

7 So for instance, the example that talks about
8 100,000 Parkinson's disease patients, you know,
9 and creating a samplings frame from them. I don't
10 think there is a population list of all patients
11 with Parkinson's disease. And therefore, there
12 will be some bias about the people not included in
13 that list and how does one go about finding those
14 people, et cetera.

15 I spoiled my own remarks by this morning
16 talking about electronic medical records and data
17 warehouses. And while indeed it is very difficult
18 to get at that data, it's getting easier. I think
19 that will be a huge shift in the next three or
20 four years.

21 But finding other places where you're more
22 likely to find patients, and actually that leads

1 me to another example, the one that talks about
2 the AMA master file. And I'm thinking that also
3 undercounts patients, right?

4 We're highly unlikely to find patients in
5 community-based health centers or in treatment
6 models where patients are more likely to be seen
7 by a general practitioner or who might not be --
8 or by a practitioner not associated with that
9 disease.

10 And increasingly, people are not being seen by
11 a doctor at all. They're being seen by a nurse
12 practitioner. They're being seen by other
13 healthcare workers. They're not going to be in
14 that master file. Now again, I don't know of a
15 better list to go from. But you know, the
16 structure of how healthcare is going today is
17 changing rapidly.

18 And I guess I'd like to see in the examples
19 there may be just even lists of possible bullet
20 points for examples for people to create on their
21 own, collecting data with new novel methods.
22 We've got FaceTime and Skype and, you know, people

1 conducting neuropsychological testing remotely.
2 So you don't actually have to send a
3 neuropsychologist out there to conduct an
4 examination.

5 I actually sat on a small panel. I think we
6 were in a third of this room, you know, on rare
7 diseases. And the pure expense of sending out the
8 same test administrator to the 300 kids who have
9 the disease all around the world almost made it
10 impossible to conduct the studies.

11 But the reality is people are having this
12 examiner sit on the other end of a camera while
13 the patient's sitting there, perhaps with someone
14 to hand them the technology.

15 But they don't have to go there, saving
16 literally thousands of dollars a day. And then,
17 you know, new untested waters. But they're coming
18 quickly.

19 There's a lot of federal funding right now
20 into using mobile phones to, again -- passive data
21 collection but also direct and indirect queuing a
22 patient, finding cognitive information. IBM,

1 Apple, Google all have already done research
2 that's shown they can predict -- they can show
3 people with mild cognitive impairment. They can
4 show people declining based upon the quality of
5 their texting. You know?

6 So these are passive models of data collection
7 that seem completely foreign on one hand. On the
8 other hand, they're working. They have much
9 better models than we do and they have access to
10 far later -- larger patient samples.

11 And one last word on that is Steve and I were
12 going back and forth on largescale data collection
13 versus random selection. And I'm not anti, you
14 know, stratified random sampling, getting there.

15 But the capabilities of getting to large
16 volumes of people, particularly if you can adjust
17 your weight for them for bias, allows all sorts of
18 subgroups to be addressed which we simply didn't
19 have the money to do. And there's access in new
20 ways.

21 And actually, it can be cheaper to collect
22 10,000 people than 30, depending upon -- or a

1 hundred or 200 or 500 -- depending on the
2 methodology. We've got a lot of methodological
3 issues to go over. But these are, you know, new
4 pathways that this discussion document will
5 eventually have to discuss as well.

6 DR. EGGERS: Thanks so much, Richard. Now,
7 Telba?

8 DR. IRONY: Hi. I'm going to allude to what
9 Laura Lee said in terms of the examples and the
10 data collection that she mentioned very rightly
11 so, that, you know, this patient information,
12 patient perspective needs to be collected and
13 submitted to the FDA only when it can influence
14 the decisions, at some decision point, if it can
15 sway the decision one way or another, that's
16 important information for the FDA purposes.

17 So I think the examples could illustrate that
18 in a way and, you know, have an example, for
19 instance, when you will collect patient
20 information to inform the design of a clinical
21 trial. In that case, you will maybe collect
22 information that will tell what are the best

1 endpoints that are relevant to patients. What is
2 the clinically meaningful difference that you want
3 to detect? So how would you collect that kind of
4 information?

5 There is another purpose that I see is to
6 inform benefit-risk determinations. For instance,
7 the clinically meaningful difference for a
8 treatment that have very low risk can be different
9 than the clinically meaningful difference for a
10 treatment of high risk. You will want more effect
11 for a high risk treatment than for a low risk
12 treatment.

13 Now, how do you determine that? It's a very
14 difficult thing to be determined. But the patient
15 can inform that. You know, the patient that lives
16 with the disease can tell if the burden of the
17 disease is so high that they are willing to take
18 more risks. So they can inform the FDA so we will
19 give a very good information on our determination.

20 So these will be good examples to get in the
21 guidance because, depending on the information you
22 are gathering, you have different ways to collect

1 it.

2 Another thing that comes to my mind is
3 labeling. Someone mentioned labeling. How would
4 that kind of information be relevant in labeling,
5 if it's relevant in labeling?

6 In some cases, it will be, particularly in the
7 cases which will help decision-making by the FDA.
8 In some situations, it might not be relevant for
9 the labeling. So these will be things that might
10 be important to get examples of that.

11 Other things that come to my mind is examples
12 on rare diseases. You know, because the disease
13 is rare, it's very difficult to collect large
14 samples.

15 But sometimes, a small sample will be
16 representative just because it's a small
17 population. So these kind of distinctions might
18 be important to get into the collection and in
19 labeling.

20 Another thing that was alluded here is real-
21 world evidence and it comes to mind, you know, how
22 to collect information from the Web or from a

1 social media using, for instance, natural language
2 processing and things. You know, this is just
3 foreseeing the future. But it's very well
4 possible, particularly for very well organized
5 patient advocacy groups.

6 So all these kind of examples will be helpful
7 if they came in the guidance because it will
8 inform people that it's not only actually the
9 guidances are not only intended for patient
10 advocacy groups.

11 It's intended to industry and it's also
12 intended to the FDA reviewers. So they will learn
13 from the guidance too. So all of this information
14 will be very well taken to be in the guidance.

15 DR. EGGERS: Thank you, Telba. Now, we have
16 Sally.

17 MS. OKUN: Thank you. Thank you so much for
18 having me here today to participate in this
19 important panel.

20 It's very clear that the FDA is not only
21 seeking broad participation for the development of
22 these guidance documents. But we've also heard

1 frequently today that the FDA is welcoming the
2 opportunity to explore novel ideas for ensuring
3 that drug development is truly patient-focused as
4 we continue into the 21st century.

5 So overall, the guidance is a comprehensive
6 discussion of traditional research methods for
7 collecting comprehensive and representative input.

8 In my opinion, the guidance actually can be
9 improved quite a bit by recognizing and
10 integrating nontraditional opportunities for
11 advancing innovation in research.

12 And by harnessing the emerging and ever
13 evolving 21st century methodologies that actually
14 are already here and being used in many cases, but
15 also that we could begin to push the boundaries
16 for expanding the scope and scale of patient
17 experience data collection methods in analytics.

18 So some might say that there isn't quite
19 enough experience using these novel data
20 collection models and analytics for regulatory
21 decision-making. You know what? I think that's
22 all the more reason for us to ensure that the

1 guidance includes these examples of nontraditional
2 approaches, so that these methods can be
3 considered and discussed with the FDA.

4 They could be potentially tried, if given the
5 right environments, and the experience could be
6 gained and we could begin to learn how best to
7 harness the power of these.

8 So if I were going to think of a few high
9 level concepts that I'd like to suggest we could
10 be thinking about including in this first
11 guidance, I'd say we need to think about expanding
12 the volume of patient experience data by using
13 online research-focused platforms and Web-based
14 and mobile-enabled networks.

15 This opens up opportunities to reach much
16 larger numbers of patients using current and
17 rapidly emerging technologies that are really
18 increasingly part of people's everyday lives.
19 Technology approaches support increased efficiency
20 and timeliness and can even improve the targeting
21 for subpopulations and diversity through strategic
22 engagement models.

1 I would also set the expectation for rigor
2 with novel data collection. You know, just
3 because it's novel doesn't mean we relax our
4 requirements on rigorous methodological
5 considerations.

6 So it is possible to integrate systematic and
7 methodological processes to collect patient
8 experience data in environments that provide
9 convenience for the patients by fitting into their
10 real-world experiences.

11 You know, we've actually had a research
12 collaboration with PatientsLikeMe and FDA for the
13 last 18 or 19 months now. And a lot of that work
14 has been spent simply studying the characteristics
15 of this novel patient experience data in order for
16 FDA to better understand how it might be useful
17 for regulatory purposes.

18 So the work is beginning and the work is
19 actually underway and I think we need to find ways
20 of continuing that to help other researchers start
21 to expand this work.

22 We need to challenge researchers to explore

1 new methods to validate patient experience data
2 collected from novel environments.

3 And I'll use another example that we have
4 done. We had a cohort of 600 consented
5 PatientsLikeMe members with multiple sclerosis and
6 we were able to identify them within a claims data
7 environment and to validate the diagnosis they
8 gave us in that claims data environment.

9 So it was an opportunity for us to use sort of
10 a novel approach to validating what patient-
11 reported information against what was known in an
12 accepted real world evidence environment.

13 Encourage innovative study designs that
14 include novel environments where patient
15 experience data can be longitudinally collected.
16 And we heard a lot of that this morning. And I
17 really want to enforce that.

18 Much of the representativeness of the real
19 world experience of patients happens over time.
20 And much of the experience that patients have
21 don't happen within the clinical site environment.
22 So we miss a lot of the kinds of things that we

1 should be collecting on a regular basis. Patient
2 networks can help support a longitudinal design.
3 Virtual trials are another opportunity that we
4 should be exploring.

5 We've recently done one with the Duke ALS
6 clinic where patients with ALS were able to remain
7 at home, do the data collection, connect with the
8 study sites over the -- excuse me, over the phone
9 or during Skype interviewing.

10 And then, they only had to go to the clinical
11 environment twice throughout the entire study.
12 The timeliness of it, the convenience for patients
13 was remarkable and the satisfaction was high and
14 retention was also high.

15 Finally, I would say to encourage
16 collaboration. We've heard that also -- across
17 data collectors and data holders to ensure that
18 gaps in one data source might actually be filled
19 by another collaborator's data source.

20 Collaboration offers greater efficiency by
21 reducing the number of duplicative studies. We
22 heard Richard talk about the 40 simultaneous

1 studies being done in fatigue earlier this
2 morning.

3 So in summary, I would suggest pushing the
4 boundaries beyond traditional methods and
5 analytics does require us to step outside of our
6 comfort zone.

7 Many sponsors and other stakeholders may be
8 reticent to explore novel patient experience data
9 collection without explicit examples to look to in
10 the guidance. So even if they're nascent, even if
11 they're still emerging, even if we still are
12 learning, they should be at least discussed in the
13 guidance as possibilities.

14 So I strongly encourage FDA to ensure that the
15 patient-focused drug development guidance are
16 relevant to 21st century patient experiences and
17 inclusive of examples that demonstrate current and
18 rapidly emerging 21st century technologies. Thank
19 you.

20 DR. EGGERS: Thank you very much, Sally. And
21 finally, we have Elizabeth.

22 DR. STUART: Great. Thank you so much for

1 having me. Many of my comments are going to echo
2 other things that we've heard and I want to first
3 say that I agree that having examples in the
4 document will be inordinately helpful in making
5 things concrete.

6 I serve on a panel for PCORI and I find that
7 often there can be discussions that are very high
8 level and theoretical that people might sort of
9 disagree about different issues. But then, once
10 we sit and talk about a specific case study,
11 there's much broader agreement.

12 So I think examples sometimes actually help
13 people realize that maybe they actually do really
14 believe the same thing kind of when you get into
15 specifics. So I think examples can really be
16 crucial in that way.

17 So one of the methods that's talked about in
18 the document is purposive sampling. And I want to
19 posit that I think the selection of examples
20 should be thought of in a purposively sampled kind
21 of way. So we'll use one the approaches that's
22 actually being proposed in general.

1 So one type of purposive sample is called
2 deliberately heterogeneous sampling. And when you
3 try to do a deliberately heterogeneous sample, you
4 sort of think about what are the factors that
5 matter that we want to make sure we have
6 representativeness over.

7 And so, I was sort of thinking, well, what are
8 those factors for selecting examples. Some of the
9 things I thought of were the sort of spectrum of
10 the goals of the study, so whether it's at a stage
11 of just measured developments, sort of
12 understanding the course of disease, whether it's
13 for an efficacy endpoint. Those are very
14 different goals. Might want to think about having
15 heterogeneity in those.

16 Another would be size and heterogeneity of the
17 populations under study. So for example, a rare
18 disease versus a more common disease. Another
19 might be chronic disease versus acute.

20 We heard earlier examples of sort of some
21 differences that arise based on that sort of type
22 of disease. Similarly, another factor might be

1 the length of the disease course. Is this
2 something that people have for six months or
3 something they have for five years?

4 And then, finally, one that's sort of near and
5 dear to my heart is -- especially as a
6 statistician, is sort of how much are you worried
7 about unobserved differences between the sample
8 and the population.

9 And so, you know, a sample of 30 people that
10 we've heard about might be highly problematic in
11 some scenarios where you're really worried that
12 those people are very self-selected in
13 unobservable ways but might be perfectly fine in
14 another scenario where they really are believed to
15 be representative.

16 And so, I think, you know, sort of thinking
17 through where does that sample come from. So I
18 just would sort of posit that FDA could sort of
19 think about what are the factors that really
20 should be considered or shown in the examples and
21 then make sure to kind of cover those.

22 And I think the key is that one size won't fit

1 all and we need examples that will fit that. And
2 so, then I just wanted to make a couple other
3 points that are more on the sort of sort of
4 slightly bigger picture comments.

5 First is just to make a sort of obvious point
6 that has been alluded to. If data on a population
7 is actually available, a non-representative sample
8 can be made to look more representative and
9 therefore presumably more generalizable with
10 respect to the observed factors.

11 So then, there's really two issues we need to
12 think about. One is what factors are observed,
13 and I'll come back to that. And then, two, how
14 worried are we about unobserved?

15 And that gets back to my comment about 30. A
16 sample size of 30 is much more concerning if we
17 really think that they are just highly different
18 and more motivated or whatever than the rest of
19 the population.

20 So then, we need to think about what
21 population data is available and what measures or
22 characteristics are available on that population.

1 So we really ideally would like to be in scenarios
2 where we have good, high quality measures on the
3 sample and the population. And again, I think
4 sort of showing diversity of scenarios like that
5 would be useful in the examples.

6 I worked in one. I sort of straddle public
7 health and education and public policy and I
8 worked in one example in Head Start, so early
9 childhood education. And I had two datasets, a
10 sample and a population. They each had 400
11 measures. But only seven of them were measured
12 consistently between those two. That is not a
13 good scenario to be in.

14 So we need to also move towards models of sort
15 of if you're running a study, try to get
16 comparable data with some population of interest
17 that's already available.

18 And then, I just want to conclude with two
19 other quick notes that again build on other
20 points. I think it will be important in the
21 examples to show innovative designs. You know, I
22 think there's often -- I work a lot in non-

1 experimental designs. And sometimes, there's an
2 immediate, like, oh, there's no way we can collect
3 a random sample. And so, people then sort of shut
4 down and go to like the other extreme.

5 And I think showing specific examples of kind
6 of compromised designs or innovative, maybe two-
7 stage designs, hybrid designs they're sometimes
8 called, can be really useful for sort of raising
9 people's awareness of the possibilities that might
10 exist and sort of not just it's either random or
11 it's not random, but really what are some
12 possibilities between that.

13 And then, finally, I just want to note that,
14 again, I straddle fields. And these conversations
15 are happening in so many different fields right
16 now. We heard a little earlier about, you know,
17 political polling and the public policy sort of
18 world, economics, online research.

19 And I would just encourage more meetings like
20 this, that I think do a great job of bringing
21 people from these different fields together
22 because really lots of different areas are

1 struggling with the same issues. And there's no
2 sense -- there's no reason, you know, we should be
3 in different silos.

4 DR. EGGERS: Thank you very much. And thank
5 you to all the panelists for giving a lot of great
6 ideas that would take years to fully flesh out.

7 I want to move now into the discussion and
8 focus it in on a couple of the bullets because I
9 think that collectively you have answered question
10 one about the thoughts and the examples in there.
11 You've given -- and you've certainly answered
12 number four.

13 When we asked you to think both pitfalls and
14 novel ideas, all of you have jumped to the novel -
15 - the novel approaches. And that's very useful.

16 So then what I want to focus in on then is the
17 third bullet here about some of the common
18 challenges in study design or implementation or
19 analysis that might be useful to address through
20 additional examples where we flesh out what the
21 situation was, why it might be problematic from a
22 regulatory perspective and how we might address

1 that challenge.

2 I'm going to put up a scenario as an example.
3 Now don't worry. This is not springing this on
4 the panelists. They were sent this earlier.

5 But we're looking for a response to a
6 situation like -- described like this, in a
7 vignette that would accompany -- that could
8 accompany an eventual guidance that spells out a
9 situation that has a methodological limitation or
10 unforeseen challenge to it.

11 So in this case, the situation that the
12 researchers, for an unspecified study goal, used a
13 probability sampling scheme to send out a survey.
14 But the response rate was low and the submitted
15 report included only the results and demographics
16 of the responders but not information on the non-
17 responders.

18 So then, this scenario further goes through
19 and outlines what makes that a potential
20 regulatory concern, to main concerns. One is the
21 representativeness of the study participants to
22 the target patient population and then the risk of

1 nonresponse bias, people who respond may
2 systematically differ from those who do not.

3 And so, then it gets into some more of the
4 sampling issues about whether this is functionally
5 a nonprobability sample. I think it was Kai who
6 mentioned this weighting adjustment. I don't
7 think that was mentioned as a methodological issue
8 before. But Kai mentioned that earlier today.
9 Anyway, it's a methodological issue.

10 And then, we thought through some practical
11 solutions, both to increase the participation rate
12 and then to factor in the potential for
13 nonresponse through a pre-specified analysis plan
14 and then through having to consider modifying
15 sampling approaches, if necessary.

16 So this is the type of information we thought
17 might be useful to illustrate fleshing it out a
18 little bit more and keeping it hypothetical as an
19 appended scenario or a vignette.

20 So I just -- so understand that we could model
21 lots of situations, including the innovative types
22 of approaches that you have mentioned in your

1 panel responses, but just as a style and as a
2 first response or first think-aloud to this
3 scenario. I'll open it up for any thoughts on its
4 utility or on what would have to be further
5 explained. Go ahead, April.

6 DR. NAEGELI: I think scenarios like this are
7 great. They would be perfect. Also taking a step
8 back and thinking about the survey itself, were
9 patients involved in developing the survey.

10 Did they feel like a valued contributor to it?
11 Was it asking sensitive questions that maybe
12 patients didn't want to necessarily respond to?
13 So doing some pilot testing of that nature would
14 be helpful as well.

15 DR. EGGERS: Anyone else? Elizabeth? Or no,
16 Sally?

17 MS. OKUN: I think one of the things that
18 stands out to me is that we don't know enough
19 really to sort of suggest, you know, how it might
20 improve in some way.

21 So if surveys were sent out and what method
22 was used to send them out, if there were ways of

1 being able to sort of have a pre-specified
2 analysis plan, it would really require you to
3 think a little bit about who you were sort of
4 ultimately trying to target.

5 And I think the scenario itself is useful in
6 sort of breaking things down. But I think it
7 lacks sufficient information to give you enough to
8 sort of sink your teeth into.

9 So I felt like I was left here feeling like,
10 well, I'm assuming they didn't necessarily use the
11 latest technological approaches to getting the
12 survey out. I'm assuming they maybe didn't put it
13 on an iPhone. I'm assuming that maybe it wasn't
14 something that was going to be convenient and fit
15 into the lives of the persons they were trying to
16 reach.

17 So those would be my initial reactions, that
18 if we were to put something like this into the
19 document, that it provides sufficient information
20 that really sort of suggests here's -- yes, we
21 could get to a practical solution.

22 But we have to know a little bit about what

1 they didn't do particularly well at the start.

2 DR. EGGERS: Okay. So let me ask you, before
3 we go to Elizabeth, could this be written up? And
4 we get overwhelmed.

5 So could this be written up in a scenario that
6 is a page to two pages and be useful and still
7 account for the things that you're suggesting?

8 MS. OKUN: Oh, absolutely. Yeah. I mean, it
9 could still remain bulleted. But it could provide
10 in each bullet just a slight bit more information
11 about the methods that were used and some of the
12 other, you know, kind of thinking that went into
13 it.

14 I think one of the things also, coming from
15 where I come from, one of the things that we think
16 about and that we integrate into everything we do
17 is really thinking about an overall engagement
18 strategy from start to finish.

19 And so, that not only includes how do we get
20 the people we want to, you know, respond to what
21 we're trying to have them respond to, but then how
22 do we ultimately figure out, for those people we

1 didn't get, what is it that we need to figure out
2 to reach them at the next point in time that we're
3 trying to reach them.

4 So I think, you know, this is the sort of
5 thing that I don't think researchers think about
6 quite frequently enough, that you're not just
7 trying to recruit people to get at your survey,
8 but you're also trying to learn from the
9 experience of that survey in order to be able to
10 improve the opportunity to gather better data
11 every time you do it again and again.

12 DR. EGGERS: Okay. And we'll go with
13 Elizabeth?

14 DR. STUART: Yeah. I think a similar feeling
15 of like I think this could work fleshed out. And
16 some of the things that I would have liked to see
17 fleshed out are first the goal of this survey.

18 So it wasn't clear to me if this was we're
19 just trying to learn about patients or if it's
20 for, you know, an outcome efficacy, treatment
21 control, effectiveness. And those would be very
22 different considerations, I think.

1 And then, the other thing I would like to
2 flesh out builds on one of my earlier comments
3 about sort of what do we observe versus what do we
4 not observe on these people and sort of what data
5 is available on the non-respondents -- well, on
6 the respondents and on the non-respondents and
7 maybe even have two sort of sub-scenarios, one
8 where there's very limited data on the non-
9 respondents, which might be common in some
10 situations.

11 And so, there you might really want to think
12 about sensitivity analyses to assess sensitivity
13 to an unobserved difference versus another
14 scenario where maybe there's really good registry
15 data or some other really high quality sort of
16 baseline data on the non-respondents so then --
17 like these weighing approaches rely on having high
18 quality, observed variables that you can adjust
19 for.

20 And so, maybe kind of two scenarios, one where
21 you feel like that's a reasonable assumption and
22 then one where it feels much iffier. And then,

1 you can cite, you know, there's like the National
2 Research Council recommendations on missing data
3 and it kind of could fit into all of that.

4 DR. EGGERS: Okay.

5 DR. STUART: But yeah, I certainly would want
6 those sorts of issues fleshed out more.

7 DR. EGGERS: Great. We'll go with Telba, if
8 you had some, if Telba had something and then
9 Richard and then Susan.

10 DR. IRONY: Just had -- yeah, I think it's a
11 little bit more, you know, according to what
12 Elizabeth said because for me -- to me, all these
13 data collection, the purpose, the objective of the
14 survey is fundamental because depending on what is
15 the objective, you know, you might be worried
16 about the bias or not in this case.

17 And also, fleshing out and giving concrete
18 examples. For instance, let's say that the non-
19 responders are because, you know, people are
20 working. So you get the non-responders are the
21 busy people and the people who respond to survey
22 are the people that are less busy. Does it impact

1 the disease experience or not?

2 You know, it comes to missing at random,
3 missing completely at random and missing not at
4 random, all these three things. And in some
5 cases, you can correct for that and in some cases
6 you cannot. There is no way to correct. So these
7 are important.

8 But you only think about this when you get
9 more concrete examples. So I think one of each
10 would be for instance missing at random, not at
11 random or completely at random, that will be
12 important.

13 DR. EGGERS: Now, these last two, is this
14 still going to fit into our two-page --

15 DR. STUART: I think we can honestly, yeah.
16 And part of it might be even just --

17 DR. GERSHON: I would --

18 DR. STUART: -- like a little simple -- like I
19 do a lot of work in mental health where depression
20 might be a concern, where you really worry about
21 not missing a random. So even just having a
22 specific here's a scenario where we're really

1 worried about not missing at random and then some
2 references on where to go --

3 DR. EGGERS: Yeah. Great.

4 DR. STUART: -- here's a scenario where
5 probably missing at random is more believable and
6 move forward.

7 DR. EGGERS: Yeah. All right. Richard, and
8 then we'll go with Susan and then I want to make
9 sure we have some time for Q&A.

10 DR. GERSHON: So similarly, using really small
11 print, keeping within the two pages, I would
12 actually add a fourth blue band.

13 DR. EGGERS: Okay.

14 DR. GERSHON: And that could be how could this
15 situation have been avoided in the first place
16 potentially.

17 DR. EGGERS: All right.

18 DR. GERSHON: Because I think actually that
19 would have helped me the most in looking at this.
20 Some of the things we've mentioned before. You've
21 got to have demographics data. Minimum data you
22 need from non-respondents. Otherwise, weighting

1 falls somewhere between voodoo science and highly
2 respected. And without that minimum demographic
3 set, it is definitely in the voodoo science side.

4 But that would help people in planning to
5 better realize what they could be going for. And
6 response rates are all over the place nowadays.

7 You know, people think I've got 11 percent.
8 Well, I'm at the national average for this. There
9 are people who get 70 and 80 percent and there are
10 people who keep people responding continuously for
11 years and others who can't get them to respond
12 later.

13 So having examples of that and sharing that
14 amongst the community would be helpful as well.

15 DR. EGGERS: Great. Susan?

16 DR. MCCUNE: So I really like this approach
17 and I'd like to see a hybrid between kind of the
18 examples that were given already and then taking
19 it to what I see as that next step of being able
20 to take what you've provided as kind of a
21 situation and then -- and I know that there are an
22 enormous number of examples that you could spend

1 forever going through.

2 But I think with the examples you have and
3 then some additional examples based on what we've
4 heard today in terms of different diseases,
5 different populations, different rare diseases,
6 you know, all of that, pediatrics, all of the
7 things that we've been talking about today, having
8 some examples of being able to then utilize the
9 practical solutions that we've been talking about
10 in terms of innovative designs and all of the
11 tools that have been so far mentioned today.

12 And some of those might be very different,
13 depending on the population or the question that
14 you are actually studying or the situation that
15 you've presented.

16 And I think that would be for me very helpful
17 to understand where I might be able to use a
18 particular practical solution more efficiently
19 than potentially in another case.

20 DR. EGGERS: Great. Thank you. So working in
21 the novel approaches ideas through some of these
22 more practical, situational-based examples. I'm

1 going to open it up to see if there's any
2 questions from the floor.

3 And while I do, you know if you were at our
4 patient-focused drug development meeting earlier,
5 you'd know that we have love show of hands.

6 So I'm going to ask for a show of hands to say
7 if -- does a scenario like this that takes the
8 concepts and puts them into a story, would that be
9 helpful? Is it worth the effort that it would
10 probably require to do that? Show of hands if
11 that would be helpful to stakeholders like you.
12 Okay. Near most, yes.

13 So I think then you've been able to give some
14 input, even if you don't come to the mic. But if
15 you would like to come to the mic and offer
16 something more concrete, feel free. Richard, go
17 ahead.

18 AUDIENCE QUESTION AND ANSWER

19 DR. GERSHON: I won't walk over to the mic.
20 Two things. One is perhaps the FDA would
21 entertain people submitting scenarios to help with
22 the burden because frankly people I think in the

1 audience could -- unfortunately, those of us
2 sitting up here -- really could help come up with
3 some of these. And I'd like to actually respond
4 to someone from the previous session and the
5 Alpha-1 person.

6 And I hope by my disagreeing with you, you'll
7 actually be appreciative. And that is you
8 indicated that, you know, we're dependent on you
9 representing patient groups. And I'm really
10 struck by this proceeding by wanting to agree with
11 you but then vehemently disagreeing with you.

12 I think this discussion document indicates
13 that the FDA and researchers are dependent on you.
14 We are dependent on patients.

15 And I think that this guidance and the -- you
16 know, the predecessor legislation is demonstrating
17 that indeed this process is dependent on patients
18 and maybe that wasn't a prevailing thought in the
19 past, but it is a prevailing thought now.

20 DR. EGGERS: Thank you so much. And we'll go
21 here with a question or comment.

22 DR. GILLESPIE: Okay. Hi. My name is Barbara

1 Gillespie. I'm an adult nephrologist at the
2 University of North Carolina. I'm at Covance, a
3 CRO that runs clinical trials. I'm also on the
4 board of directors at the Kidney Health
5 Initiative.

6 You know, I think this is a fantastic meeting.
7 But there are people who are not here in the room
8 because they don't exist. And so, for example,
9 you know, we all know diabetes affects 12 million
10 Americans.

11 Chronic kidney disease affects 15 million.
12 Half of that is from diabetic kidney disease. But
13 there is no one consolidated diabetic kidney
14 disease patient group that I'm aware of.

15 So yes, I think the patient advocacy groups in
16 the room, you know, it's important for them to
17 have their say. But for groups like that, who's
18 speaking on their behalf? I would say the same
19 for end-stage renal dialysis patients.

20 And so, that's kind of, you know, an issue in
21 nephrology that we have to bear and we're trying
22 to deal with. But I have a concern. And you

1 know, I've worked with sponsors for the last 12
2 years in developing protocol design, feasibility
3 and executing trials and have always thought it's
4 important to get the patient feedback, even the
5 feedback from study coordinators and dialysis
6 nurses.

7 I guess what I'm concerned about is the risk
8 that sponsors take. It takes time and money to
9 get patient feedback, a lot of paperwork. And
10 even if you do it electronically, there's still a
11 lot of effort that goes into there.

12 And it's hard to convince sponsor executives
13 to invest this time and money without clearly
14 defining a return on investment. So hopefully
15 that return on investment will be to support an
16 approval or add to the label.

17 But what about the risk of the data showing
18 from patient preferences showing it's neutral or
19 even negative or even discordant with the hard
20 outcomes that we're finding and even that prove
21 positive.

22 For example, fatigue. I'm also part of the

1 SONG initiative in dialysis patients where we're
2 trying to come up with a standardized set of
3 outcomes. Fatigue is important to patients. It's
4 important to us clinicians.

5 But it's hard to tell a patient that your
6 fatigue improved by two units and it's
7 statistically significant. What is that really
8 saying to the patient? Especially in something
9 like dialysis?

10 Fatigue improvement at month one, six and 12
11 after they start dialysis, there's so many
12 compounding variables. What was their hemoglobin
13 level? Comorbidities? How many times were they
14 in the hospital? We've listed a couple other
15 limitations with gathering patient data and
16 patient preferences.

17 And so, you know, I looked to the pediatrician
18 there on the panel. In pediatric drug
19 development, there have been regulatory incentives
20 to study kids. And I think it's even a negative -
21 - even if you do a negative trial, that sponsor
22 will still receive a patent exclusivity extension.

1 So can we think about regulatory incentives
2 for sponsors, given the patient input, for the
3 same scenario? Because I think there is a risk,
4 time, money and a neutral or negative outcome in
5 getting patient preferences.

6 The other thing I want to point out that, you
7 know, sponsors also have to, and will, invest time
8 and money in doing health economic outcomes
9 research because they want to achieve
10 reimbursement success too, right?

11 They want to show payers and CMS that this is
12 worth it. So again, what are the regulatory
13 incentives that we can put in place to help
14 sponsors make these decisions and investments?

15 DR. EGGERS: Thank you. So to tie it back in
16 here, what I'm hearing is a scenario that could
17 address when the findings weren't quite what one
18 had hoped or still learnings but it might not be
19 directly able to support what it was intended to
20 support, either how -- you know, how was that
21 handled or what else could that have been used for
22 or how maybe -- how did it yield a shift in

1 direction to something that is still useful. So,
2 thank you. Is there anybody -- Sally?

3 MS. OKUN: I just want to make a quick comment
4 on that.

5 I think it's critically important that we
6 actually do encourage the reporting of findings
7 that didn't come out as one expected or hoped for
8 because those sorts of negative outcomes actually
9 can help us learn about the kinds of things that
10 maybe were didn't do in ways that might have been
11 better to complement data sources with each other.

12 But I think it's oftentimes that kind of
13 information that we don't share. So I would
14 encourage that.

15 DR. EGGERS: Thanks, Sally. We have Theresa.

16 DR. MULLIN: So following up on Richard's
17 encouraging or mentioning that people could offer
18 examples, I mean, I think it would be very
19 helpful, and to follow up on Sally's point, that
20 we try to include more about nontraditional, and
21 Elizabeth's, to innovative, nontraditional
22 methods.

1 It probably would be helpful too, since you
2 have a great deal of expertise with those methods,
3 and maybe even giving examples of what would be
4 for you now obvious pitfalls or things to avoid
5 because if we're going to try to encourage the use
6 of nontraditional methods, you don't want people
7 to get burnt by making mistakes.

8 And I think, quite frankly, that FDA sees a
9 lot of maybe not great ideas that have been
10 pursued and money's been spent on them.

11 So to the extent that a guidance can not be
12 looking in the crystal ball and figuring out
13 everything that can work, you know, all that
14 innovation, but examples of what to not do, I
15 mean, some just kind of sensible things from based
16 on your experience of what not to do when you're
17 pursuing novel methods.

18 DR. EGGERS: We'll go with Meena as our final
19 question.

20 DR. KHARE: I have a comment from my recent
21 experience on the situation and then you move into
22 the how to improve. But the first line it says,

1 okay, survey of patients you send out. Again, it
2 goes back to the first session we had. What is
3 your frame where you are getting the data?

4 And the second bullet says, okay, researchers
5 note that the response rate is low. Why it is
6 low? It's very important to look at it because we
7 have recent experience that I was working on.

8 It's the same database, same EMA list of
9 frames and we use it in provider surveys. One of
10 them has a very high response rate and also what
11 is the topic, what your objective is because the
12 other one, we had a big problem with unlocatables.

13 Fifty percent of them, you couldn't locate.
14 People moved, providers, patients. So you have to
15 build in all of that and then figure out why it is
16 low before you go into it and then you look into
17 what information is available and how do you
18 adjust your final estimate.

19 Are those estimates any good? What is the
20 quality of it? And we struggle with it all the
21 time. And one of them really I was surprised when
22 we started looking. After data collection, I was

1 involved. And I said, well, why it is low, in
2 teens? And you have the same survey, the same
3 database, another survey has very high response
4 rate.

5 And then, it turned out to be there were half
6 of them were not locatable. And then, there was
7 an eligibility criteria. That dropped further
8 down. So then, what you're left with is a very,
9 very small sample.

10 So those things have to be built in when we
11 are trying to improve and maybe it should be done
12 as you're collecting data, at the same time look
13 at it. And then, after the first small sample,
14 and see what's going on.

15 DR. EGGERS: Great. Thank you.

16 DR. KHARE: Even with the new technology, that
17 everything is on the social media. But you can't
18 follow up. A lot of providers move, patients
19 move. So mobility is another problem.

20 DR. EGGERS: Thank you.

21 DR. KHARE: And cellphone, it's a really big
22 problem because you're -- people move around and

1 keep the same cellphone. So which area you are
2 sampling from? Is it from New York or California?
3 So, thank you.

4 DR. EGGERS: Great. Thanks. Any final
5 questions here on the panel from my FDA
6 colleagues? Okay. I do want to thank Megan
7 Moncur who has been sitting down at the end who
8 has been -- I drew the short stick to be up here
9 at the podium. But she has done a tremendous
10 amount of work.

11 So thank you so much. Did you have any final
12 questions you wanted to ask? Anything come to
13 mind? Oh, okay. All right.

14 MS. MONCUR: let me try again. Thank you.
15 No, I don't.

16 DR. EGGERS: All right. We are on time and we
17 will take a 15-minute break and then come for our
18 final session, which will -- our final facilitated
19 session which will identify key themes. So thank
20 you to the panelists for the great suggestions.

21 (Applause.)

22 (Whereupon, the foregoing went off the record

1 at 2:44 p.m., and went back on the record at
2 3:02 p.m.)

3 DR. EGGERS: Sorry. If you want to work your
4 way back to your seats, we'll get started in a few
5 minutes. All right. Is everyone working your way
6 back to your seats? Because we are on the last
7 sessions before you can get back on the Beltway or
8 the Metro, which I hope is working more smoothly
9 this afternoon.

10 Okay. Before we get into our session, we had
11 a new addition to our FDA panel for this
12 afternoon. So I just wanted to let Tejashri
13 introduce yourself.

14 DR. PUROHIT-SHETH: Sure. I'm Tejashri
15 Purohit-Sheth and I'm from the Office of Tissues
16 and Advanced Therapies in CBER, FDA.

17 SESSION IV: IDENTIFYING KEY THEMES AND NEXT STEPS

18 DR. EGGERS: Great. Thank you. Okay. So we
19 are in the final session, identifying key themes
20 and next steps. And we'll start by asking the
21 panelists to introduce themselves. They're not in
22 the order on the slide. But I don't think anyone

1 has been on the order of the slide. So it's
2 probably -- I think it's just a random placement.
3 So we'll start with Theresa. We'll start with
4 Elektra. Introduce yourself and then we'll --

5 DR. PAPADOPOULOS: Hi. I'm Elektra
6 Papadopoulos. I'm associate director for clinical
7 outcome assessments staff in the Office of New
8 Drugs, CDER.

9 MS. BERLIN: Conny Berlin, from Novartis. I'm
10 the head of qualitative safety and epidemiology.

11 MS. MCCLEARY: Hi. I'm Kim McCleary. I'm
12 managing director and currently the acting
13 executive director of FasterCures, which is a
14 center of the Milliken Institute.

15 MS. EREMENCO: Hi. I'm Sonja Eremenco. I'm
16 associated director of the Patient-Reported
17 Outcome Consortium at the Critical Path Institute.

18 DR. WITTEN: Celia Witten, deputy director for
19 CBER at FDA, the Center for Biologics and
20 Evaluation Research.

21 DR. EGGERS: Thank you all. Theresa, do you
22 want to introduce yourself?

1 DR. MULLIN: Theresa Mullin. I direct the
2 Office of Strategic Programs in the FDA Center for
3 Drugs.

4 DR. EGGERS: Okay. Great. So the purpose of
5 this session is to wrap up what we heard and how
6 we hear our FDA colleagues, what the key message
7 is you're taking away, and our external
8 stakeholder representatives up here, what you're
9 taking away from the meeting today.

10 But then, we're asking you to add on a few
11 pieces about looking at the overall discussion
12 document and really this discussion document in
13 the context of being the first in a series.

14 What are your thoughts about it being as a
15 document the right scope, the right direction, the
16 right balance to help stakeholders? And also,
17 what are your key recommendations for FDA moving
18 forward?

19 So it's a little bit heavier ask for our
20 external stakeholder representatives. But we will
21 start with Theresa to reflect on the key takeaways
22 that you -- that you've heard for today.

1 MODERATED PANEL DISCUSSION

2 DR. MULLIN: Okay. Thank you, Sara. So my
3 major takeaways were that I think we did a pretty
4 good job with the discussion draft, trying to be
5 comprehensive enough and make it accessible enough
6 and usable, which is what we set out to do.

7 But one thing I think I learned today is that
8 I didn't appreciate what a good vantage point FDA
9 has in seeing what looks to us to be sort of an
10 evolution and you might even say revolution in
11 terms of the involvement of patients and the role
12 that patient advocacy groups and others can play
13 in the drug development.

14 And I think patient groups help to go beyond
15 that period of the ecosystem. And that we've come
16 to learn through the previous five years too that
17 there are evolving approaches. There's a lot of
18 innovation going on. There are modes of
19 collaboration going on that we can't even
20 anticipate yet.

21 And so, we don't think that there's a single
22 use case or a single scenario for how a document

1 like this would be used. We really were trying to
2 make sure that this new and critical player, which
3 is becoming more of a larger and recognized as an
4 important player, also can have an understanding
5 and working with others, but have a good working
6 understanding of the kinds of things that we would
7 be looking to see in a development of endpoints
8 and information that we can use to better
9 understand what matters the most to patients.

10 So perhaps we need to try to do even a better
11 job. We have worked on this, to set the stage in
12 the beginning of the guidance to convey that, that
13 this is trying to provide the information for
14 across all the stakeholders and including ones
15 that who have not traditionally been in drug
16 development as much as they probably will be going
17 forward. So that's one point.

18 And my second one was probably related to
19 that, that we were encouraged to be -- that
20 openness to new methods, but making sure that
21 they're going to deliver reliable results. And I
22 think that's something we very much appreciate.

1 We've been encouraged to consider adding
2 examples with more nontraditional methods or
3 innovative designs and to encourage folks to
4 consider those and maybe come in and talk to us
5 about it before proceeding very far to see if they
6 can get that aligned with what we'd be looking
7 for.

8 And another area, my third area -- I think
9 Sara mentioned three areas. So I'm on my third
10 one now, that maybe we can also make clearer where
11 we would see that things might be developed that
12 would be sharable, ideally would be sharable.

13 It's non-proprietary information that would be
14 of interest to the community in a disease area,
15 for example, and maybe others that could be
16 sharable more publicly versus what should be
17 submitted to FDA to support FDA decision-making.
18 It could be the information might be used in both
19 ways.

20 But some information we would want to see to
21 support decision-making. Others might be very
22 helpful to advance development of drugs in an area

1 if it were shared with the community. So I'll
2 stop there.

3 DR. EGGERS: Thank you very much, Theresa.
4 And now, Elektra?

5 DR. PAPADOPOULOS: So my big three takeaways
6 are, you know, the importance of clearly defining
7 the research objectives for your patient input,
8 the importance of, you know, understanding how the
9 FDA will use the patient experience information
10 when we receive it and the importance for the FDA
11 to remain aware. And so, I'll try to take those
12 each.

13 So with regard to the research objectives, I
14 think, you know, it's very important to -- and
15 we've heard just to kind of take a step back at
16 the outset before delving into the research and
17 what is it that we want to accomplish, what is the
18 ultimate regulatory use of the research and this
19 is what's really needed to spur investment and
20 incentivize people to undertake this research
21 because it can be obviously resource-intensive.

22 And so, the idea of starting with the end in

1 mind is very relevant here and making sure that
2 we're asking the right questions. And so, this is
3 going to take dialogue between the FDA and our
4 external stakeholders and we want this to be
5 collaborative.

6 We want it to be in the precompetitive setting
7 so that we can have information sharing,
8 minimizing burden to patients, regulators,
9 industry and others and duplication of efforts.

10 And this is really where the patient
11 organizations play a crucial role as the conveners
12 and supporters of these activities, not to say
13 that patient organizations can do all the work by
14 themselves. No, it's going to take a village.

15 But they can really play a crucial role in
16 this process. And we want to avoid ultimately the
17 scenario where work has to be redone to -- because
18 we've used a wrong method or a target population
19 for our research question.

20 So the next one is, you know, there's a big
21 need and desire for our stakeholders to understand
22 what is FDA going to do with this information.

1 And again, I think once we're clear on this, this
2 will allow groups who are sort of working on
3 similar issues, perhaps in different disease
4 areas, but working on some more sort of issues and
5 research questions to really learn from each
6 other.

7 And with that, the hope is that with this
8 learning, regulatory submissions will improve in
9 sort of a continuous learning environment. And I
10 think with the website that we're planning to
11 open, this transparency and sharing will really
12 assist in this.

13 Then, the last one is awareness, awareness.
14 We need to be aware of -- there are innumerable
15 resources and databases, consortia and we've heard
16 several mentioned today that can be leveraged.

17 And we also need to stay aware of the
18 technologies, social media, real-world evidence,
19 mobile technologies, passive and active data,
20 virtual research, et cetera, et cetera.

21 And so, all of these things, we need to be
22 aware of. We need to make sure that we remain

1 open to the evolution and we want, you know, to
2 really avoid any implication that we're inflexible
3 or that we're not staying ahead of a really
4 rapidly evolving field and science and technology.
5 And so, I think we need to continue to be aware
6 and to be nimble and adapt to the evolution. And
7 that's all I had.

8 DR. EGGERS: Thank you, Elektra. And now,
9 Conny?

10 MS. BERLIN: Okay. So I think, like my
11 speakers before, I would say also to me the
12 workshop has shown how much all the different
13 stakeholders really appreciate FDA's enormous
14 effort here to develop a guidance for patient-
15 focused drug development and how much also such a
16 workshop gives us the opportunity for a very early
17 dialogue and how much and how many new ideas we
18 have got today and which you now have the really
19 hard job to really incorporate this into the
20 guidance, I would think.

21 I think the guidance has shown us before
22 already and given us a very good idea what a

1 systematic and factored approach could be for
2 patient-focused drug development.

3 And I think what has been emphasized,
4 especially today in all the discussions, is the
5 collaborative aspect and how much all the
6 different stakeholders, be it industry or
7 regulators or patients, are really behind that
8 idea of collecting patient experience data and use
9 these data for better decision-making. I think
10 that was really my first takeaway.

11 And then, my second takeaway, as also said
12 before, is that the high importance of what is
13 really the goal of the patient experience data,
14 how to use these data.

15 And I guess for me, really the key driving
16 aspect here can be the benefit-risk from FDA
17 because this is for me the final goal. And I
18 think also as you have written in your guidance,
19 we all aim to have very good benefit-risk
20 assessment at time of submission and for the
21 approval.

22 And I think the benefit-risk can even help us

1 to identify what are the research questions, what
2 really are our objectives and help us discussing
3 very early what are the first aspects to consider
4 in developing this roadmap.

5 I think that has been mentioned several times
6 today, that it would be good to have a roadmap for
7 the full development program where we see at what
8 time we might want to use and collect what type of
9 patient experience data for what purpose.

10 And we have heard different aspects like
11 informing the clinical trial design or patient
12 preference information. And I guess these early
13 discussions will help us then go through the full
14 lifecycle, which also means that it's not the one-
15 time discussion.

16 But we probably need to have several
17 discussions during the lifecycle. And we need to
18 have that together with the patients. And I think
19 we have heard how much even our patient
20 organizations are encouraged to run their own
21 studies which might be even very important and
22 helpful to not duplicate or replicate studies.

1 And what I find also really important as a
2 takeaway message here is to maybe even more
3 emphasize the role of the patient in this journey
4 and in running the studies.

5 That is what we have learned also in the IMI
6 PREFER project which is a public-private
7 partnership to develop recommendations for patient
8 elicitation for benefit-risk assessment.

9 There, patients tell us very often how -- that
10 they don't want to be considered only as data
11 providers, but want to play an active part and
12 really be equal partners, which means that they
13 want to be at the table when we discuss the
14 research question, when we discuss the study
15 design because they would know best whether, for
16 instance, a focus group discussion really works
17 for them or whether they would feel much more
18 convenient with individual discussions at the
19 beginning, for instance. Yeah, I guess I stop
20 here and hand over now.

21 DR. EGGERS: Great. Thanks. Kim?

22 MS. MCCLEARY: Great. I'll echo a lot of the

1 other panelists. Thanks to the FDA for this
2 opportunity to sit on this panel and for this
3 workshop and for the extraordinary work that's
4 gone into the guidance and just the embrace of
5 this evolution, as Theresa called it, or maybe
6 even a revolution in the way that patients are
7 reflected in the totality of medical product
8 development and regulatory decision-making.

9 And I was struck as I was sitting listening to
10 the earlier sessions about just this widening
11 aperture and this opportunity that we're now at
12 with patient perspectives where we've gone, you
13 know, taking kind of a bigger step back from there
14 being really no involvement of patients in
15 settings like this to in the sort of days
16 following the HIV crisis when the HIV activists
17 sort of insisted on a seat at the table and there
18 might be a single patient representative or
19 advocate sitting on an ad com in the scope of a
20 single product decision to with PDUFA-V and the
21 PFDD meetings having kind of a convenience sample,
22 if you will, of people who could come to White Oak

1 or some other place in the D.C. area for 24
2 meetings that you all hosted and nine that have
3 been held by externally led groups and hearing
4 maybe a little bit more about sort of the burdens
5 of the condition, the burdens of the therapies,
6 the unmet medical need to now this guidance really
7 shaping how do we collect a more comprehensive and
8 sort of evolving story about what it means to be a
9 patient with a certain diagnosis and all of the
10 things that impact health and outcomes and
11 longevity when you have that diagnosis or perhaps
12 collection of diagnoses, as we were reminded.

13 I think it's important as we think about this
14 to connect back to something, Theresa, you said
15 very early in the day and that I've heard you say
16 on many other occasions, that one of the really
17 important outcomes of the PFDD meetings was a
18 recognition by FDA of how many times the domains
19 that the patients were talking about in the
20 setting of those meetings were maybe disconnected
21 from the things that they knew sponsors were
22 studying.

1 And if we think about this guidance, this
2 series of guidances as being a bit of a roadmap to
3 help reduce the frequency with which that occurs
4 and to sort of step back at that level and say,
5 okay, what are we really trying to accomplish.

6 And we could get way down into the, you know,
7 types of case examples we use. But that's really
8 what this is all about, right? And so, I think
9 about it in that context.

10 So my second takeaway is really to echo a
11 comment that Annie Kennedy made from the floor
12 about the audience for this document not just
13 being the patient organizations or the
14 sophisticated ones that know to come here on the
15 December 18th workshop. But this is really for
16 all of us.

17 And also, to clarify that the burden for
18 conducting this type of work that will inform all
19 of these different steps in a long and expensive
20 and time- and resource-intensive process of
21 developing new medical products is a shared burden
22 that we all will face and that, as others have

1 said, needs to be collaborative.

2 So I see the great value in this draft
3 guidance and the guidance that will follow as
4 being a platform for sort of level-setting the
5 conversation, for the glossary and the appendices
6 and the methods that are described in it to really
7 give us a shared vernacular and a way of
8 understanding what we're shooting at in terms of
9 collecting this evidence and why we would do it
10 and being real clear in our collaborative
11 initiatives about talking through all of these
12 different aspects.

13 And for that reason, I see this as being, you
14 know, extremely valuable and well done in terms of
15 the structure of the document itself, starting out
16 at a pretty high level with kind of a series of
17 questions and answers in pretty plain language and
18 then the progression through the document, getting
19 increasingly more academic and detailed in terms
20 of the specific methods and how you would go about
21 collecting this evidence and for what purposes it
22 might be used.

1 And I think you did a really great job of
2 breaking down the concepts so you don't need
3 Benicio Del Toro to come in as the code breaker
4 and tell you like what is meant by, you know, this
5 document.

6 But we did hear maybe from some of our
7 industry colleagues that they thought it was at
8 too high a level for patients. And I'm probably
9 not a good representative of the patient community
10 because I've been in too many of these meetings.

11 So perhaps it's an opportunity for FDA to
12 involve some of the patients from either the
13 patient rep program or the patient engagement
14 advisory committee or somehow to maybe do a pre-
15 vetting when you do have the draft document itself
16 to make sure that it does have a readability
17 factor for those who may not be as familiar with
18 this language and lingo.

19 The third takeaway I had is I think one of the
20 greatest challenges that you'll face, in addition
21 to incorporating all of the feedback you'll get
22 and have already gotten, is striking the

1 appropriate balance between enough detail that we
2 all have kind of a good understanding about what
3 we're shooting at with not being either overly
4 prescriptive to kind of chill the evolution of new
5 methods and nontraditional ways of doing some of
6 this work or to make it appear so complex and
7 daunting that people just say thank you, no, I'm
8 not going to do this. It looks impossible.

9 And if we got wrapped around, you know,
10 concepts of representativeness and making sure
11 we've got every single perspective captured or
12 eliminating any source of bias or getting to the
13 perfect design, that would certainly just stop us
14 all in our tracks because we'll never quite get
15 there.

16 And then, I think you've also got the added
17 complexity in every therapeutic area the
18 challenges are going to be somewhat different.
19 Some have a very high velocity of change and a
20 study done one month might be really kind of not
21 needed six months later because you've had a new
22 treatment or a new diagnostic entered the market

1 and it changes things for patients.

2 So we can't let the perfect be the enemy of
3 the good I guess is the phrase. And also thinking
4 about this as you really start to walk through how
5 do you get this information to FDA, that there
6 might be some scenarios in which it's not a study-
7 by-study basis.

8 But you're really trying to create kind of a
9 collection of sources of really, again, going back
10 and understanding what is it like to be a patient
11 with this condition. What are the important
12 choices that they are going to be making?

13 And it may be more a body of evidence that
14 accumulates over time than just something that's
15 much more of a snapshot, so leaving open that
16 opportunity as well. And with that, I'll turn it
17 over to Sonya.

18 DR. EGGERS: All right. Thank you so much,
19 Kim. And then, Sonya?

20 MS. EREMENCO: Hello. Good afternoon. Thank
21 you so much for this opportunity to speak on this
22 panel today. And I really appreciated what the

1 previous panels have said and the panelists who
2 spoke earlier in the sessions today.

3 I just -- so I'll touch on some of the key
4 takeaways that I had and also some of kind of
5 related to the fourth question about kind of
6 thinking about the bigger picture and how all the
7 pieces fit together.

8 So we heard a lot about collaboration. We
9 thought that's a really key point. And myself,
10 coming from the Critical Path Institute, that's
11 kind of our motto as well. We're all about
12 collaboration.

13 And I kind of saw it in a couple of different
14 ways. One was collaborating around developing
15 perhaps new measures, new instruments, collecting
16 data in a collaborative way. But I also thought
17 of ways to collaborate to reduce the burden on
18 patients.

19 I think we heard in a couple different
20 sessions that we don't want to do new data
21 collection all the time for all of our conditions.
22 That's just going to exacerbate the problem that

1 we've seen in the past with redundant studies and
2 that we really need to find ways to either use
3 data we already have in new ways and perhaps
4 collect data from new sources, like social media.

5 I think we heard in a couple of different
6 cases, social media can be a source of data. It's
7 a nontraditional source and there are some caveats
8 and challenges and you have to be careful about
9 the authenticity of who's providing that data.

10 But it's something that could be considered as
11 a way to get a better sense of the patient
12 perspective and the patient experience without
13 having to do the traditional methods. So I think
14 it will be a really important thing for FDA
15 colleagues to think about, you know, how can we
16 incorporate some of these nontraditional methods
17 not just examples in this guidance but as part of
18 the options of methods to use.

19 I think by putting them in the guidance as
20 options, it kind of gives not just an impression
21 but it kind of makes them more acceptable. Right
22 now, by focusing just on traditional methods, I

1 think it will make researchers and industry
2 hesitant to use some of these newer nontraditional
3 methods because it's not kind of blessed in the
4 guidance. So it's not kind of seen as acceptable.

5 So I think that's something that's really
6 important because there is so much existing data
7 out there and there should be ways that we can
8 leverage it and use it moving forward for patient
9 experience data.

10 So my second point was about technology. I
11 kind of touched on that a little bit. But I want
12 to talk a little bit more about that too. I think
13 we heard it touched on in some of the earlier
14 sessions. But it's not just because it's novel
15 and new and fun.

16 But clearly, with some segments of the
17 population, that might be the only way we can
18 reach them. We're not going to be able to reach
19 younger people using traditional telephone
20 surveys. You know, we need to find the methods
21 that will match the populations that we're trying
22 to reach. And I think that there could be a

1 little bit of expansion in the guidance around
2 ways to use technology for the purpose of patient
3 experience data.

4 And in terms of moving -- kind of moving
5 forward and the bigger picture, one of the things
6 that occurred to me as I was reading the
7 discussion document was really a better
8 understanding of the context of this guidance in
9 terms of how it fits -- you know, how it relates
10 to the PRO guidance, how patient experience data
11 relates to PRO data because I felt like in this
12 current draft, that distinction wasn't really
13 clear or the way that they complement each other
14 wasn't really clear.

15 And I think that's really important,
16 especially to I would say the researchers and
17 industry who might find the way that it's phrased
18 in this guidance a little bit -- there's a lot of
19 overlap. Let me put it that way.

20 And I think for us to really understand, you
21 know, where does it fit and kind of which guidance
22 do we need to be looking at when we're working

1 with either PRO or patient experience data, when
2 we're looking at symptoms and when we're looking
3 at function that really fall into both categories.

4 So I think maybe adding a little bit more
5 about the context and the background to the
6 guidance and also currently section one outlines
7 the four guidances that are part of this aspect of
8 the PDUFA and the 21st Century Cures.

9 And I think it will probably be necessary to
10 repeat that outline in all of the guidances just
11 to reiterate here's the structure, here's where
12 the different sections are, here's where to find
13 the information that you might be looking for.
14 So, that's all for me.

15 DR. EGGERS: All right. Thank you so much,
16 Sonja. And we have Celia.

17 DR. WITTEN: Yes. Thank you. It's been an
18 interesting day and I'd like to thank all of the
19 participants in this meeting and to the organizers
20 for inviting me. So I will be brief because
21 there's obviously some common themes in these
22 remarks.

1 But to some extent, some of these may be
2 things that we'll want to address in this guidance
3 and some of them maybe are comments that we want
4 to think about in other parts of this entire
5 project. So they may not speak specifically just
6 to this guidance.

7 But one relates to the audience and I think
8 that's already been discussed, that this is
9 intended for multiple stakeholder groups, both
10 patient groups and industry and it may be that
11 some further consideration of that, you know,
12 needs to be made or put in the introduction or
13 thought about when the guidance gets developed.

14 There's been a lot of discussion about the
15 research objectives being important. And I think
16 it's important for a number of reasons. But some
17 of the commenters have also talked about how the
18 data will be used or how it could be used.

19 And I think that's important when you really
20 can't talk about research objectives without
21 thinking about how you're going to use the data.
22 So I think that we did get the suggestion that

1 there might be some examples of what the impact of
2 some of these could be and that might be something
3 to consider.

4 And then, separate questions which may not be
5 for this guidance but certainly are something for
6 us to think about, is how data from one of these
7 studies would be submitted or shared with FDA.

8 You know, if it's part of a formal submission,
9 I think it's a little more intuitive what we'd
10 expect. But if it's for some other purpose,
11 exactly how do we expect to have that shared with
12 us.

13 Certainly I think that's important to think
14 about and one of the previous speakers referred to
15 this guidance as an ocean of opportunity, which I
16 think is a good thing. But it also might be good
17 for us to, you know, give some examples that would
18 explain.

19 As one of the speakers on this panel said,
20 this guidance will probably be helpful and others
21 have said throughout the day this guidance will be
22 helpful hopefully in enhancing collaborations and

1 hopefully also eliminating duplication of work by
2 establishing a common vernacular for what these
3 studies should be or could be.

4 And then, the last thing I want to mention is
5 just about examples. So there were two kinds of
6 examples that were discussed during that session
7 and also earlier in the day, methodological
8 examples and examples of the impact of the study,
9 which are really two different things.

10 But I think they are related. And there was a
11 great example in one of the morning talks, or one
12 of the earlier talks anyway, about quantitative
13 versus qualitative studies, which I think very
14 well incorporated the importance of thinking about
15 your research objectives when you think about
16 formulating your study design.

17 And maybe that is an important concept that we
18 need to think about a little bit more. So that is
19 all I had to say. Thank you.

20 DR. EGGERS: All right. Great. Did anyone's
21 comments spur additional thinking by those of you
22 as you heard each of you go through your comments?

1 Did it spark any new thoughts? Go ahead.

2 MS. MCCLEARY: So one thing, and we talked
3 about this a bit on our prep call for this
4 session, was a lot of the conversation today just
5 -- I don't know -- emphasized the need for a
6 communications plan when this draft guidance comes
7 out and maybe it goes into the document itself or
8 along with it in the form of blog posts or
9 something from the commissioner or, you know, to
10 re-explain sort of because others are still
11 catching up with where we all are in this
12 discussion.

13 And that's going to be really important if we
14 want this to get beyond sort of the early adopters
15 or early majority.

16 DR. EGGERS: So let me follow up on that. I
17 think this would be for you and Sonya, if you --
18 even the voice blog has to assume that you're
19 connected to FDA and that you're following along
20 in this.

21 What are your thoughts on how FDA can connect
22 with people who maybe aren't in this space yet,

1 particularly for a rare disease or another
2 organization that's maybe focused on other -- on
3 patient support, but not yet focused -- but they
4 can tap into a lot of -- they have a wealth of
5 knowledge. How would we reach out to them?

6 MS. MCCLEARY: I would suggest for the -- I
7 assume you've kept registration lists for the 24
8 PFDD meetings, that, you know, blast emails,
9 because they may not get the regular emails from
10 FDA, going out through the patient rep program and
11 the 200 or so people that are part of that as
12 ambassadors to, you know, voice this and then
13 getting out to as many different areas of industry
14 because often it's, you know, regulatory or
15 clinical affairs that come to these kinds of
16 meetings.

17 And then, you talk to somebody else in the
18 same company and they don't even know what you're
19 talking about. So I think we just have to kind of
20 take a very broad-based but also targeted approach
21 and engagement for this too.

22 DR. EGGERS: Great. The same question, we had

1 -- those of you -- some of you may have
2 participated in the meeting on patient preference
3 information that was held in collaboration with
4 FDA and other academic institutions last week.

5 And there, we got a comment that there are
6 researchers who work in very similar areas who are
7 qualitative experts or other types, but they're
8 just not in this space. They're not in
9 pharmaceutical development.

10 Any thought maybe, Sonya, this is for -- oh, I
11 won't put you on the spot -- any thought on how we
12 could reach out to other researchers who could
13 also contribute?

14 Because I think we're going to find that we
15 need to build capacity in the research community
16 to help with this what we hope is the evolution to
17 come. Any thoughts?

18 MS. EREMENCO: I guess what occurs to me, and
19 this is kind of related to the earlier question
20 because it could be patient groups, it could be
21 other researchers in other areas, is potentially
22 to go to their conferences, to really seek them

1 out and either try to present there or make
2 connections that way, network with them and
3 broaden our horizons that way.

4 DR. EGGERS: Great. Okay. Go ahead, Conny.

5 MS. BERLIN: Yeah, maybe one thought. I guess
6 the more we strengthen the role of the patient
7 also in the guidance, the more industry will
8 certainly collaborate also and other patient
9 organizations weighing in here. And I guess that
10 would be also one way to communicate messages.

11 AUDIENCE QUESTION AND ANSWER

12 DR. EGGERS: Great. I'll open it up to see if
13 there are any questions. You can feel free to
14 come up. Okay.

15 So I do want to go back to the point about
16 this guidance as the first in a series of
17 guidances. I don't know if it's the only time
18 we've done it. It's not typical for FDA to put
19 out things in a series. So any more thoughts?

20 I know -- I think one of you mentioned this.
21 But would anyone else like to follow up on
22 thoughts on how we can best guide stakeholders'

1 understanding that there's more to come and that
2 this is really laying the groundwork for a lot of
3 future work to follow? Any thoughts? Go ahead,
4 Theresa.

5 DR. MULLIN: Well, I guess I don't have a lot
6 of other ideas. I think that, to Kim's point
7 earlier, and it's a very good one about putting
8 together maybe a more complete communications plan
9 involving others including people who focus on
10 communications with the right messaging.

11 You know, I think we're still dealing with the
12 bandwidth issue frankly in this space in terms of
13 our own expertise in the agency. So I think that
14 kind of slows us down a little bit. But that
15 would have been a really good thing for us to do.

16 And I think that some of the other channels
17 where I think we just need to in fact get that new
18 story. I mean, we really need to kind of put what
19 do we explain to people. What's the message of
20 what we're doing here? For the next few years,
21 we'll be repeating it and going over it. And
22 that's probably a good way and it's also part of

1 change management as well is over-communication.

2 So we're going to have to do that lot better.
3 But at things like DIA, I mean, you could think of
4 some of the large conferences which industry
5 participates a lot and we're going to have to
6 really reinforce the message there. You can think
7 of some of the other large venues where the
8 stakeholders participate and that -- so I think we
9 need a multipronged approach on it and we can do
10 that.

11 I think the point's well taken too about going
12 further, if we can, on laying out a roadmap. And
13 so, here's where it's both -- we're trying -- I
14 think what we'll try to balance is laying out a
15 roadmap but also trying to be open to innovative
16 approaches.

17 So it's not like this is the way to do it,
18 like this is the only way to do it because that's
19 contrary to the idea of allowing people to be
20 innovative. But we understand there's a tension
21 there because people really do want to in some
22 ways be told this is the way to do it. So we'll

1 have to try to figure out how to walk that and
2 balance that.

3 DR. EGGERS: Go ahead. Yeah.

4 MS. PALLADINO-KIM: So it actually leads right
5 into something I was going to bring up. So, hi.
6 Lisa Palladino-Kim. I'm from Rutgers University.
7 We have a master's in clinical trial science. I
8 think Conny was bringing it up earlier an then you
9 just mentioned it with the roadmap.

10 Just FYI, from a high level concept, the Drug
11 Information Association worked and put together an
12 actual patient engagement I guess pictorial. And
13 it actually goes through the whole drug
14 development process and they have the time points
15 of when the patient voice or patient engagement
16 can occur and actually be of benefit.

17 So that might be something to have a
18 conversation with them and use that as your high
19 level guidance to help develop your roadmap.

20 DR. EGGERS: Okay. Thank you very much. One
21 thing that hasn't been discussed much today was
22 the glossary of terms. Now, of course, you can

1 comment in the discussion -- I mean, into the
2 docket that we have available.

3 But I wanted to put and see if you had any
4 thoughts on the glossary, if you'd refreshed
5 yourself in the last few days, I'd put to the
6 external stakeholders. Was it -- as you read
7 through it, was it useful? Did it resonate with
8 you, the terms? Okay.

9 MS. BERLIN: I found it very, very useful,
10 very good. So I don't have really comments. I
11 found it very helpful.

12 DR. EGGERS: Okay. Great. Great.

13 MS. EREMENCO: I thought it was very useful as
14 well and I think it was good to reference existing
15 definitions from the best glossary and other
16 places rather than creating, you know, new
17 definitions that would just create confusion.

18 And I think the only thing that struck me was
19 there was one term that wasn't in the guidance
20 that was in the glossary. And it's something I'll
21 probably comment on in the docket just because I
22 think it's a term that probably belongs in this

1 particular guidance, as well as the future ones.
2 But it was helpful to hear earlier today that it
3 wasn't necessarily meant for just this guidance,
4 but for all of them.

5 DR. EGGERS: Okay. Thank you. Any other
6 questions from -- go ahead. Yes?

7 MR. BUSH: Yeah. Hi. Alex Bush, from Syros
8 Pharmaceuticals. We've talked a lot today about
9 the use of surveys and about patient data leading
10 ultimately to an understanding of the disease and
11 then maybe at some point an inclusion or an
12 endpoint.

13 But it never came up, the role of the patient
14 voice in the way we think about inclusion and
15 exclusion criteria. And I was wondering if that
16 was something that you're considering through the
17 development of these guidances.

18 DR. MULLIN: I mean, that's part of trial
19 logistics also. So I think that all of this works
20 in together, yes.

21 MR. BUSH: Okay. Thanks.

22 DR. EGGERS: Okay. Great. Question?

1 MR. DEWITT: Thank you. Steve DeWitt,
2 Parkinson's advocate. And I want to thank the
3 committee for all the work that's been done up to
4 this point because there's a lot that you've done
5 and I really appreciate that.

6 And I did have a question that the young lady
7 from New Jersey just spoke to about the issue of
8 regulations that exist right now on industry on
9 when they can talk to a patient and when they
10 can't.

11 And so, DIA is taking a step to try to make
12 this little model to help industry understand who
13 they can talk to and when. And I've kind of
14 always felt why couldn't they talk to me now about
15 these subjects and not be so regulated. And I
16 know that there are reasons for it for as far as
17 wanting to be too -- don't want to be too much of
18 an influence.

19 But I wonder if we took those away, if there'd
20 be more input from the community and the
21 stakeholders without those regulations. Could
22 someone respond to that?

1 DR. MULLIN: Okay. Well, let me begin by
2 saying I'm not a lawyer at FDA. It's very
3 important.

4 But I think the kind of interaction that would
5 be of concern would be construed -- would be the
6 kind of talking that would be construed as
7 marketing an unapproved product.

8 So if it's really early conversations that are
9 really marketing the product and it's unapproved,
10 that that would be objectionable.

11 The kind of interaction we're talking about
12 here is quite different I think and I think if
13 what we have been saying is if there is -- there
14 are certain kinds of communication that we do not
15 want, would not want and then there are other
16 kinds of communication and really listening that
17 we do want.

18 And that's what we're trying to cover in these
19 guidances, is what we would like to see. So it's
20 more focusing on what we really hope to see. And
21 a lot of it has to do with asking questions and
22 listening but not marketing a product that's not

1 been approved for marketing, if you know what I
2 mean. Not promoting a product that's not approved
3 for marketing.

4 DR. EGGERS: Thank you.

5 MR. DEWITT: I don't mean to speak for
6 industry. But industry itself, maybe they don't
7 want to cross that line.

8 And so, they would take a more cautious
9 approach and maybe leave out a lot of Q&A that
10 could help advance the treatments more quickly if
11 they didn't want to protect the liability
12 associated with walking that line. And so, it's
13 maybe something to look at for the future.

14 DR. MULLIN: Yeah, and maybe if they read this
15 guidance, they'll move the line as well.

16 DR. EGGERS: Go ahead, Kim.

17 MS. MCCLEARY: And you might think about in
18 the case examples that you're conceiving, maybe
19 there's one that's product -- you know, in a
20 product-specific scenario that illustrates like
21 maybe not where the line is but how close you can
22 get to it because I do think that is a point of

1 hesitation.

2 And also, you know, I think there might be
3 some leading ways. And we've had this
4 conversation about using the target product
5 profile as a platform to get early sort of
6 alignment around what are the features and
7 benefits and tradeoffs early on in a development
8 program.

9 But how much then does that create
10 expectations on the part of the patients who are
11 informing that process? Oh boy, you know, they've
12 designed -- this is going to design a drug that
13 really is what I want to have.

14 So I do think there are, you know -- it's easy
15 to say we want to foster this. But then, you get
16 down and the devil is in the details, as it always
17 is.

18 DR. EGGERS: It's an interesting concept of
19 managing patients' expectations about the data
20 being collected and the -- on the opportunities
21 that they could imagine coming from it. Did
22 someone else -- was someone else going to say

1 something?

2 MS. BERLIN: I guess, I mean, the more normal
3 it becomes that this is really data which we use
4 in the drug development process, it might be
5 really simplify the process and becoming clearer
6 with the -- I mean, the purpose is then clearer.

7 And I guess then it becomes hopefully also
8 easier to collect the data. But on the other hand
9 side, maybe you're also aware that there's still
10 quite a -- usually it takes quite a long time to
11 set up all the contracts with the patients and to
12 go through this.

13 So this is what we have learned already. This
14 is also an information which we get back from the
15 patients. But I guess we can work on this.

16 DR. EGGERS: Great. Okay. With that, I think
17 we have covered -- I'm not going to say every
18 topic we could have covered in the course of the
19 day. But it has been -- I think we're at the
20 saturation points in terms of topics and variety
21 of thoughts that are out there.

22 But this isn't the only -- I'll put another

1 plug in. This isn't the only opportunity you
2 have, especially if you are on the Web and haven't
3 had a chance to put a comment through. The
4 docket, there'll be information coming I think at
5 the end.

6 But the docket, so your recommendations not
7 just one what's in the guidance document but on
8 how we can make sure that the eventual guidance is
9 as useful to stakeholders as possible, either
10 through examples or communication plans, other
11 ways to reach people will be very helpful.

12 So I will close the end of this session and
13 we'll move it to Meghana, to Meghana who will do
14 the open public comment. Thank you very much to
15 the panelists for your thoughts.

16 (Applause.)

17 OPEN PUBLIC COMMENT

18 MS. CHALASANI: Hello again. I don't have
19 slides this time. So there's no room for
20 technical glitches. That was quite embarrassing
21 as a millennial.

22 So now, we're moving on to the open public

1 comment session of our workshop. Please keep in
2 mind that FDA will not be responding to your
3 comments during this session, but that they will
4 be transcribed and be a part of the public record.

5 Since we would like this to be a transparent
6 process, we encourage you to note any financial
7 interests that you have related to your comment.
8 If you do not have such interests, you may state
9 that for the record as well. And if you prefer
10 not to provide this information, you can still
11 provide your comments.

12 We have collected sign-up before the meeting
13 and during the break. We have nine people signed
14 up. So please be respectful for your other
15 colleagues here and stick to the two-minute limit.
16 We won't have a timer. But I will be keeping
17 track of time. So if you approach the two
18 minutes, I'll start asking you to wrap up.

19 So I'm first going to run through the order of
20 the speakers, and I'm going to apologize in
21 advance if I mispronounce your name. We have
22 Danielle Friend, Anthony Howell, Steven DeWitt,

1 Melena Anjikova (ph), Jennifer Madsen, Cheryl
2 Coon, James Valentine, John Davis and Eric Gascho.
3 So with that, I will ask Danielle Friend to come
4 to the mic, please.

5 DR. FRIEND: Good afternoon. My name is
6 Danielle Friend. I'm the director of science and
7 regulatory affairs with Biotechnology Innovation
8 Organization. BIO is the world's largest trade
9 association representing biotechnology companies
10 across academic institutions, state biotechnology
11 centers and related organizations across the
12 United States and in 30 other nations.

13 BIO thanks the Food and Drug Administration
14 for the opportunity to provide oral comments at
15 this public workshop. BIO also commends the FDA
16 for its plan for issuance of patient-focused drug
17 development guidance under 21st Century Cures Act
18 Section 3002.

19 These guidance documents will be important for
20 informing sponsors, patient organizations,
21 academic researchers and healthcare professionals
22 of the FDA's expectations for collection,

1 analysis, submission and utilization of patient
2 experience data. As the FDA begins drafting
3 guidance on these methodologies, we ask the FDA to
4 consider a couple of points, some of which were
5 mentioned today.

6 First, we ask the FDA to consider providing
7 clear opportunities to engage with the FDA as
8 stakeholders begin designing strategies and
9 studies to collect patient experience data.

10 Specifically, BIO requests that the FDA
11 specify when and how sponsors can consult with the
12 FDA during drug development regarding the conduct
13 of studies related to patient experience and the
14 incorporation of patient perspectives into
15 regulatory decisions.

16 Opportunities to engage with the FDA will be
17 important for ensuring that data collected from
18 patients accurately reflects the current patient
19 population and are appropriate to inform drug
20 development and review.

21 We also ask for flexibility in approach
22 because we are in the early stages of

1 incorporating patient experience data into the
2 drug development and review processes, BIO asks
3 that the FDA remain flexible as new approaches are
4 tested, learnings are gathered from experiences
5 and practices evolve.

6 We also ask the FDA to consider challenges
7 faced by sponsors when determining how to provide
8 patient experience information that is
9 representative of a patient population.

10 To this end, we ask that the FDA remain
11 flexible as to requirements for representing the
12 range of relevant diversity in patient
13 populations. We also encourage the FDA to promote
14 the use of technology-enabled methodologies for
15 collecting comprehensive and representative input.

16 Finally, we ask for the allowance of the use
17 of mixed method approaches. BIO asks that the FDA
18 be receptive to the use of both qualitative and
19 quantitative patient experience data for
20 regulatory decision-making.

21 We also ask that as the FDA begins drafting
22 guidance regarding methodological approaches for

1 patient-focused drug development, an emphasis be
2 placed on the utilization of the most appropriate
3 methodology as determined by the particular
4 research question at hand.

5 Thank you again for the opportunity to present
6 our views on collecting comprehensive and
7 representative input for patient-focused drug
8 development.

9 BIO would like to thank the patient
10 organizations who've developed draft guidance and
11 language for the FDA and provided their valuable
12 input on issues pertaining to patient-focused drug
13 development.

14 In addition to these comments, today BIO will
15 be submitting comments via the written -- or
16 written comments via the open docket. We also
17 look forward to working with the FDA and patient
18 organizations as well as other stakeholders in the
19 future on questions related to patient-focused
20 drug development. Thank you.

21 MS. CHALASANI: Thank you, Danielle. Next, we
22 have Anthony Howell.

1 MR. HOWELL: That's a short walk. Hi. Thank
2 you for organizing and hosting the conversations
3 today. My name is tony Howell and I am the
4 cofounder of rareLife Solutions, which is a health
5 technology company collaborating with advocacy
6 organizations and industry to build novel, online,
7 verified patient communities designed as engaging
8 and methodologically rich opportunities to collect
9 patient experience data from patients, advocates
10 and caregivers.

11 We've heard the term social media a lot today
12 and we would like the FDA to consider these novel
13 communities as distinct from social media,
14 particularly for orphan conditions.

15 Verified patient communities are pretty much
16 what they sound like, a discrete online community
17 dedicated to a particular disease or condition,
18 joined by individual patients, advocates and
19 caregivers who are impacted by that particular
20 disease or condition and whose role or status in
21 that community has been verified using voluntary
22 authorization, security tools, documentation,

1 video uploads and other third party corroboration.

2 They are distinguished from general population
3 social media sites like Facebook, Twitter,
4 Instagram, Pinterest, et cetera because of the
5 connection among its members. Verified patient
6 communities are dedicated to people coming
7 together who are motivated to make things better
8 regarding that particular condition.

9 And this connection attenuates in orphan
10 conditions where patients, advocates, caregiver
11 members and their friends and families and support
12 professionals can be some of the most
13 inspirational, knowledgeable and driven people who
14 advance research from the patient's side by, among
15 many things, sharing their experiences from their
16 relevant perspectives.

17 Verified patient communities are more like
18 registries because of the verification process
19 which in turn elevates the reliability of the data
20 collected. However, verified patient communities
21 differ from registries because they offer a more
22 engaging opportunity by coupling a social

1 component with immediate acknowledgement of the
2 data contributed. This creates a rewarding,
3 dynamic and altruistic incentive to participate in
4 the research process.

5 I'd like to briefly discuss the strengths of
6 the verified patient communities with respect to
7 verification which uses antechambers in which
8 information related to the member roll,
9 demographics and patient-reported health
10 information can be corroborated using cross-
11 matching public records, ICD codes, et cetera,
12 even two-way token authorizations used on mobile
13 phones.

14 Representativeness is addressed because they
15 are easily accessible to the individual through
16 simply signing up online which allows the common
17 or average patient to connect resulting in
18 participation from a broad cross-section of the
19 community and potentially more robust sampling
20 frames and, finally, prospective data collection
21 because they are designed exactly to do this, to
22 collect the data using mixed methods both

1 immediately and over time using passive and active
2 engagement techniques and social engagement tools
3 built directly into the verified patient
4 community.

5 We have built and recently launched a verified
6 patient community designed specifically for people
7 impacted by sickle cell disease and it serves as a
8 real-world example about how this data can be
9 collected and considered as a primary source.

10 So we would like the FDA, in drafting its
11 guidance, to consider including verified patient
12 communities as a defined source and method for
13 collecting patient experience data, distinguished
14 from social media and indicate that data from
15 verified patient communities can be considered
16 primary data.

17 We will be submitting additional specific
18 suggestions to the public document -- docket,
19 sorry. Thank you for your time and consideration.

20 MS. CHALASANI: Thank you, Tony. Next, we
21 have Steve DeWitt.

22 MR. DEWITT: I'd like to yield my time to

1 Karlin Schroeder from the Parkinson's Advocacy
2 Community and if she has a second left, I'll fill
3 it in. But I don't think she will.

4 MS. CHALASANI: Okay. Sounds good.

5 MS. SCHROEDER: So, Steve and I actually work
6 together. I'm Karlin Schroeder and the director
7 of community engagement of the Parkinson's
8 Foundation. And I'm happy to be here with a group
9 of people with Parkinson's who are advocates, so
10 Steve Dewitt, Kevin Clark and Gary Farfel (ph) are
11 here today.

12 I coordinate our Parkinson's advocates and
13 research program at the Parkinson's Foundation.
14 We train people with Parkinson's and their care
15 partners in how to team up with researchers in
16 industry, academia and government to design
17 clinical trials.

18 And I did want to just build on what Steve
19 said but also on some of the things we heard
20 earlier today. I think the methods of collecting
21 patient experience data and the methods of patient
22 engagement and research may overlap in a lot of

1 areas but are two different things that are
2 complementary of each other.

3 So I think the speaker from Novartis had said,
4 you know, it's not just giving the survey to
5 collect information from patients about their
6 experience. But it's helping patients actually --
7 and allowing patients to actually help design that
8 survey.

9 And that is sometimes where we find hesitation
10 from our industry partners is going to that next
11 level. It takes more time upfront. But you're
12 probably going to have a better survey in the end.

13 You'll have better data collected, less
14 missing data, better retention because patients
15 actually helped design that survey and helped
16 determine what questions to ask and how to phrase
17 those questions.

18 And I think maybe that's a little bit of what
19 Steve was getting at. And I think too that what
20 we have found is that, you know, we would really
21 like to see encouragement again from FDA on how to
22 do that patient engagement and research piece of

1 it, so going to the next level.

2 Coalitions like the Drug Information
3 Association, the Clinical Trials Transformation
4 Initiative and Patient-Focused Medicines
5 Development are all working on best practices for
6 patient engagement in research and I think that
7 ultimately, you know, having that supported by FDA
8 would be very helpful. I think I'll leave it at
9 that. Thank you.

10 MS. CHALASANI: Thank you. Next, we have
11 Melena Anjikova. Sorry.

12 MS. ANJIKOVA: It's not an easy name. My name
13 is Melena Anjikova and I'm a senior research
14 scientist at Evidera, a research organization.
15 And today, I would like to make a comment from our
16 patient-centered research group which reflects our
17 first impression from reading the draft
18 guidelines.

19 So, first, we want to thank the agency for the
20 tremendous amount of effort to prepare for this
21 first public meeting to discuss the patient-
22 focused drug development guidance. We do

1 recognize the agency has led a number of
2 innovative patient-centered efforts over the past
3 decade, including the growth and expansion of the
4 patient representative program, the patient
5 network, voice of the patient meetings, device
6 patient preference initiative and also, most
7 recently, the establishment of the patient
8 advisory board.

9 These and other efforts have communicated a
10 vision for a paradigm of drug development where
11 patients are truly at the center of the design and
12 evaluation of medical products. The establishment
13 of the patient-focused drug development guidance
14 is a critical and important next step to
15 communicate this vision and drive change.

16 In the first guidance, which will set the
17 stage for the series of other guidance on drug
18 development, we do recommend the agency outline a
19 framework for the use of patient experience data
20 in medical product development.

21 As stakeholders navigate this new paradigm, we
22 urge the agency to consider a clear mechanism for

1 stakeholders to engage with the agency in the
2 context of both precompetitive and the NDA
3 submissions. Thank you.

4 MS. CHALASANI: Thank you. Next, we have
5 Jennifer Madsen.

6 MS. MADSEN: Hi. I'm Jen Madsen. I'm with
7 Food Allergy Research and Education. Thank you
8 for the opportunity to share our comments on the
9 topic of patient-focused drug development. I
10 represent Food Allergy Research and Education, the
11 leading organization offering life, health and
12 hope to the 15 million Americans living with food
13 allergies.

14 Food allergies affect 1 in 13 children.
15 That's two in every classroom. And the number is
16 increasing rapidly, with 50 percent growth from
17 1997 to 2011.

18 Food allergy is a life-altering and
19 potentially life-threatening disease in which the
20 body's immune system mistakenly targets a harmless
21 food protein, an allergen, as a threat and attacks
22 it. This causes an allergic reaction which can

1 range from mild to severe. Anaphylaxis is a
2 severe allergic reaction that comes on quickly and
3 may cause death.

4 An estimated 40 percent of children with food
5 allergies have experienced a severe or life-
6 threatening reaction. And a recent study by FARE
7 Health -- not associated with the fair -- found
8 that emergency room visits for anaphylaxis have
9 skyrocketed, growing by nearly 400 percent in the
10 past decade.

11 Anaphylaxis often begins within minutes after
12 a person eats a problem food. In some cases,
13 symptoms may begin hours later. Those symptoms
14 affect one or more of several body systems -- the
15 lungs, heart, throat, mouth, skin and gut.

16 We're learning that food allergies are a
17 constellation of disorders involving epigenetic
18 changes to the immune system, the human
19 microbiome, environmental changes and increasing
20 exposure to allergens over the lifespan.

21 Many factors have contributed to changing
22 human immunity over the last 50 years, including

1 higher use of vaccines, antibiotics and Cesarean
2 sections and the lack of exposure to breast milk,
3 parasites, sunlight and allergenic foods.

4 Research that FARE is funding at 30 centers
5 across the country who collectively treat about
6 80,000 patients is helping us understand the
7 molecular mechanisms of allergic reactions and
8 identify potential targets for new
9 immunotherapies.

10 Two companies are currently in Phase III
11 trials developing immunotherapies, one oral and
12 another delivered for a patch for peanut allergy.

13 We are pleased to see this evolution of food
14 allergy, which previously has been a disease with
15 no therapeutic options other than avoiding the
16 problem food and carrying epinephrine, which can
17 save lives but does not prevent future reactions.

18 From the data we've seen so far, it's apparent
19 that these products probably won't work for every
20 patient with a food allergy. But that's not
21 surprising and, in our view, products that work
22 for some patients, even if not for all of them,

1 still should be approved by the agency.

2 Peanut allergies are the most common type of
3 food allergy and we believe there may be multiple
4 molecular mechanisms driving their allergic
5 response to peanuts. There are seven more
6 allergen candidates and some of those like tree
7 nuts and fish contain multiple species, different
8 antigens.

9 Assuming we can characterize the antigen's
10 impact on the immune system at the molecular level
11 and find molecules that block the response, it's
12 entirely possible that we could be in a position
13 to treat allegories to multiple foods with the
14 same treatment. This would be an exciting
15 breakthrough for patients who are allergic to
16 multipole foods.

17 Just as FDA has recently approved a drug based
18 on a tumor's biomarker without regard to tumor --
19 the tumor's original location, FARE hopes that the
20 agency will consider a similar personalized
21 medicine approach with respect to food allergy
22 immunotherapies. Drugs that target a specific

1 cytokine, regardless of the food that triggered
2 the cytokine's production, should not require
3 clinical trials for each food individually.

4 We're also continually challenged by a lack of
5 biomarkers that can be used as endpoints in
6 clinical trials. Currently the only definitive
7 diagnostic test for food allergy is an oral food
8 challenge which involves giving the patient the
9 very food they're allergic to and waiting to see
10 what happens. Fear of food challenges limits
11 enrollment in clinical trials and slows down the
12 pace of scientific discovery.

13 We hope to engage in dialogue with FDA to find
14 more patient friendly endpoints.

15 MS. CHALASANI: Thank you, Jen.

16 MS. MADSEN: Thank you very much.

17 MS. CHALASANI: Thank you. Thank you. Next,
18 we have Cheryl Coon.

19 DR. COON: Hello. I'm Cheryl Coon. I'm a
20 consultant to the pharmaceutical industry. I'm a
21 principal at Outcometrix. The discussion document
22 and then the discussion itself today took a deep

1 dive into methods for generating patient-centered
2 data.

3 But what's missing is the big picture of why
4 we're collecting the data and how it's going to be
5 used. Several folks mentioned today the sponsor
6 perspective and at least two people asked about
7 the incentive for sponsors to undertake such work.

8 You have representatives from the outcomes
9 team at different pharmaceutical companies
10 represented here today. And they'll be going back
11 to their teams having to convince their clinical
12 development team or regulatory leads that these
13 activities are valuable.

14 So the guidance would be more useful for
15 convincing sponsors to use these methods if
16 guidance number one went into detail into what
17 questions these methods would answer and what
18 decisions would be based on these data.

19 Is it for internal purposes when designing a
20 clinical trial protocol? Or is it for submission
21 to the FDA to support the appropriateness of an
22 endpoint hierarchy to patients? Going back to the

1 slide that Theresa Mullin presented this morning
2 on the drug development timeline, where in the
3 timeline would these data be used?

4 Would it be at a Type C meeting? Would it be
5 at an end of Phase II meeting? Where are these
6 touchpoints between the sponsors and the FDA to
7 submit these type of data?

8 And then, this could all be made more concrete
9 if incorporated into the examples throughout the
10 document of the type of conversations and
11 decisions that will be made after the data are
12 analyzed. Thank you.

13 MS. CHALASANI: Thank you. Next, we have
14 James Valentine.

15 MR. VALENTINE: Good afternoon. My name is
16 James Valentine and I am a drug development
17 regulatory attorney. However, before I was ever
18 practicing law, I was at FDA working on pre-PDUFA-
19 V and pre-21st Century Cures approaches to
20 incorporating patient input into the agency's
21 regulatory decision-making.

22 I now represent over 20 patient advocacy

1 organizations, as well as numerous medical product
2 developers to help them provide patient experience
3 data to FDA and have utilized almost every method
4 highlighted in the discussion document to do so.
5 I commend the agency for this very thoughtful
6 document, especially providing a broad range of
7 tools for the PFDD toolbox.

8 Today, I would like to raise two points that I
9 feel should be considered in developing this PFDD
10 guidance. First, the discussion document, as well
11 as the panel one and two discussions, called for
12 clear research goals and objectives.

13 I agree that this is critical, as it informs
14 who do you ask and how do you collect it.
15 However, before stakeholders can set their
16 research objectives, it would be important to have
17 insights into what FDA's regulatory needs are and
18 the agency's thoughts about the needs of the drug
19 development enterprise.

20 Therefore, the guidance should not only
21 provide decision-making factors to match research
22 questions to "fit for purpose" research methods,

1 but also do the same between common research
2 questions and the areas of drug development and
3 FDA decision-making that the answers to those
4 questions could help inform.

5 This would be an area ripe for examples based
6 off the agency's experiences from working with
7 those patient advocacy organizations and sponsors
8 who have been the tip of the spear, piloting the
9 methods under consideration.

10 Second, I have had the pleasure of being
11 involved in 13 patient-focused drug development
12 meetings, both FDA-hosted and externally led,
13 several that I've moderated.

14 What I've observed is that much of FDA's
15 learnings about patient experiences and
16 preferences come from FDA representatives'
17 participation in the in-person meeting.

18 While the voice of the patient reports and
19 draft benefit-risk frameworks are valuable for
20 memorializing the input and help FDA reviewers
21 reference that patient experience data at the time
22 of decision-making, it is impossible for the full

1 context of a patient's own words to be
2 communicated in a summary report.

3 So while the discussion document provides
4 methods for in-person input, the PFDD guidance
5 should also include externally led PFDD meetings
6 and should encourage FDA officials to attend these
7 meetings so they have a venue to hear directly
8 from actual patients and caregivers as one way to
9 receive patient experience data, another tool in
10 the toolbox.

11 Thank you for the opportunity to share some
12 initial thoughts. I look forward to submitting
13 some more comprehensive written comments to the
14 docket.

15 MS. CHALASANI: Thank you, James. Next, we
16 have John Davis. John Davis? No? Okay, next and
17 finally we have Eric Gascho.

18 MR. GASCHO: Good afternoon. My name is Eric
19 Gascho. I'm the vice president -- it's okay.
20 I've been called worse. I'm the vice president of
21 policy and government affairs for the National
22 Health Council and I would really like to thank

1 FDA for a very thoughtful set of documents that
2 were put out.

3 It is clear that the agency is valuing the
4 patient perspective and really will see the voice
5 of the patient become a much more integral part of
6 your work over the course of the next five years,
7 and it already has been. So really excited about
8 that.

9 Much of the focus today has been on the
10 discussion document. But I also want to commend
11 you on the glossary. We think that it's really
12 important to be all singing from the same songbook
13 and starting out with a set of commonly accepted
14 nomenclature to make sure that all the documents
15 are consistent throughout the process.

16 One thing that I want to highlight from the
17 document is about leveraging third party
18 templates, checklists and guidances and updating
19 the approach as you go on. I think this is really
20 important for a few reasons. I think it shows two
21 themes that are prevalent throughout the document.

22 One is a collaborative approach with the

1 community. We think it's really important not
2 creating the wheel. And two, it shows that the
3 FDA really understands that this is an evolving
4 science and will be -- the processes will be
5 evolving as the science evolves as well. So,
6 commend you there.

7 A few things I want to highlight, and much of
8 what I planned on talking about has been covered
9 today. But one is on the fact that this is not
10 going into the methods for COAs and for patient
11 preferences.

12 And you referenced the patient preference work
13 that was done by CDRH. And it's still not clear
14 if this is CDER formally acknowledging that
15 document. So certainly more clarity there we
16 think would be really important.

17 And one other thing that was mentioned earlier
18 was about the -- about FDA labels. Wanted to
19 point out, while I understand that the key
20 audience for FDA labels are patients and
21 providers, to really understand that there are
22 other decision-makers who use those as well,

1 namely for coverage and payment and value
2 determinations and really understanding that if
3 not on the label, there needs to be additional
4 documentation to really make it clear how the
5 patient perspective was used in decision-making we
6 think will make their decision-making much easier
7 and have the voice of the patient injected into
8 that as well.

9 So thank you. We will obviously be submitting
10 written comments, including a set of
11 recommendations that come from all of our members.
12 So, thank you.

13 MS. CHALASANI: Thank you, Eric. Now, I'd
14 like to invite Laura Lee Johnson for closing
15 remarks.

16 CLOSING REMARKS

17 DR. JOHNSON: Thank you, everybody. So most
18 of what we heard today and what we are trying to
19 focus on is that these documents are pragmatic.
20 What's being proposed is feasible and user-
21 friendly. And apologies to anyone who thought we
22 were going to try to put everything on the patient

1 groups.

2 But one thing I want you all to note also as
3 an apology in advance that the draft guidance
4 comes out this way. Our actual template, the
5 title says guidance for industry. If you look
6 really hard, it's guidance for FDA staff and
7 industry.

8 So do not be dissuaded and think that the
9 information we're putting out is only for those
10 few stakeholder groups. As many have pointed out,
11 this is for a much wider range of stakeholders and
12 that is part of what we are focusing and
13 emphasizing here.

14 We also want to emphasize that every situation
15 is unique and nothing is perfect. But you know, I
16 don't have the slide that I use in some of my
17 presentations where I have a picture of a limbo
18 stick that's maybe three inches off the ground.
19 Like I'm not sure how the person is even able to
20 get underneath it.

21 But then, also you have those high jumps and
22 pole vaults. And usually our work, what we see is

1 going to fall somewhere in between there. But we
2 need do to have some boundaries. It can't be so
3 perfect, everything that's necessary and decided
4 that nobody can ever achieve it because, yes,
5 that's never -- we're not going to make any
6 progress. But also, there does need to be a
7 floor.

8 And so, that's what we are trying to work on
9 and there's been a huge description today of the
10 many different types of patient experience data,
11 the many types of stakeholders. And also, the
12 many different ways to collect that information
13 and data. We heard the word hybrid quite a bit
14 and I think that we'll probably be seeing that
15 work its way into the guidance also.

16 But also, really that collaborative part and
17 that a huge emphasis on ground preparation for the
18 building of whatever is to come and to make sure
19 that that prep is solid enough that when people
20 start living in and working in that building, that
21 it's going to stand up to the tests.

22 But there's not just one approach. I ask you

1 all to please send us your examples. We can try
2 to think of examples to use in the guidance. But
3 we're also trying to think of, well, who's going
4 to get mad at us, like how can we kind of hide all
5 of the good and the bad.

6 So if you all have specific examples we can
7 put in or that maybe get shared in a common area,
8 that is also useful. And that's true also for any
9 templates, checklists, other documents that people
10 have found useful. If your organizations are
11 willing to share, we can try to find and
12 facilitate a sharing place for that.

13 So you know, I mentioned this morning on
14 behalf of Elektra, but also we had more than 30
15 different FDA people working on different working
16 groups for this across not only the Center for
17 Drugs and Center for Biologics.

18 But we also have a collaboration with our
19 other centers at FDA. So CDER and CBER are the
20 people covered under that PDUFA commitment later.
21 But we do not work in isolation. We work in a
22 large group effort across multiple different

1 centers beyond that.

2 So our questions to you, I'm going to go into
3 a little more detail than what others have, is in
4 fact down to what is that level of detail. We
5 can't write a textbook.

6 But how do we balance the detail and
7 comprehensiveness in that usability and that user
8 friendliness? Is it okay with what we had for
9 this workshop today? Is it something that we need
10 to add an additional layer? And if you think an
11 additional layer is needed, please tell us what it
12 should be and how to present it.

13 Should it be in an appendix? Where should it
14 go? What should be there? Or you can say this is
15 great, don't change it. Just slap a cover page on
16 it and go. That's an okay comment too, wherever
17 you think it's necessary.

18 What is the document structure for this first
19 guidance? Do you like how we broke it out for
20 this workshop where it's really kind of three
21 documents related together? Do you want one thing
22 that's cohesive in a single area? So let us know

1 about that.

2 Is there missing content? Is there
3 corrections to the current content that we have?
4 Is it clear FDA's open to discussion of the
5 methods described in other methods?

6 So I hear some folks saying yes, it's clear
7 you're open. And other folks are like, I'm still
8 worried about my regulatory group inside my
9 company. So talk a little bit about that and how
10 you think we can kind of solution these issues.

11 Now, another focus and point I want to bring
12 up here, we talked about the glossary. So there
13 was a meeting I was at and they brought up
14 something called the devil's dictionary where the
15 definition of a dictionary of a malevolent
16 literary device for cramping the growth of a
17 language and making it hard and inelastic.

18 This is clearly not our intent. So think
19 about are the proposed draft definitions clear and
20 do they really serve to facilitate the dialogue.
21 What I thought I heard today was yes. But again,
22 make sure that we're not backing out way into

1 something that will make life more difficult
2 instead of a solid good path forward.

3 What are the most important time points?
4 Cheryl Coon brought this up and I was like, oh
5 good, that's on my slide. What are the time
6 points where FDA input could be maximally helpful?

7 So for those of you all who are creating this
8 information, for those of you all who are working
9 in organizations that might be using it and for
10 anybody else, what are the touchpoints that you
11 would like to see the most? Let us know those.

12 So we have our internal thoughts on this. But
13 you may come up with something that could be even
14 more useful or that we could elaborate on more.
15 Are there any other additional external resources
16 for us to consider?

17 But also, if you have any information,
18 documents, thoughts, comments, anything else to
19 share, please submit it -- I'm going to emphasize
20 the word quickly here -- to the public docket for
21 this meeting.

22 And also, please share this with other

1 groups in different ways. So I know before I came
2 to the U.S. government, I knew everything there
3 was about this Federal Register and the
4 notification process, which is I didn't know it
5 existed at all.

6 So please, if there are groups that you think
7 may not have heard about this, please share this
8 with them and help us also be able to broaden
9 because this is the first of four workshops that
10 we'll be holding underneath this part of that
11 commitment so that we can have robust interactions
12 in the future too.

13 Now, this morning, Pujita and others mentioned
14 our due date is Friday, February 16th at 11:59
15 p.m. Eastern. But this is our new difficulty,
16 which is we now have to get our first guidance on
17 the street probably June of 2018.

18 It's a long process to go from we think the
19 draft is ready to actually publishing the draft,
20 which means if you can submit your comments in the
21 next, say, two to three weeks, there's a far
22 higher likelihood we are going to be able to use

1 it as we are actually getting that draft guidance
2 ready to go.

3 So we had the option. We could say there's
4 only a 30-day comment period. But we realized
5 there are a lot of holidays and vacations perhaps
6 planned in the next few weeks. So we went with a
7 60-day comment period.

8 We will do our best if you submit it at 11:58
9 p.m. Eastern on the 16th of February to include
10 your thoughts in the draft. But understand we
11 also have a lot of review responsibilities.

12 Everybody involved with this, this is
13 something we do because it's passionate for us.
14 But we also carry full review loads as well. So
15 we will try. But it might be that it makes it
16 into a final guidance. It might be that it gets
17 rolled into other guidances as well.

18 So how do you actually do this? So you have
19 this picture here. And when I checked at the
20 break, we still only had zero comments received.
21 So please, start submitting them. You click on
22 this little button.

1 So if you see kind of the link to the Federal
2 Register notice, this is the page. You click on
3 comment now. When you click on comment now,
4 you're going to get a page that looks like this.

5 And you literally just put in your comment.
6 You can upload files. You can put in your name
7 and contact information on behalf a third party,
8 select different things. But it's actually now a
9 pretty nice Web form that folks can use.

10 So again, our draft guidance, which will also
11 have a federal comment period through this same
12 type of docket, is expected to go out June 2018.
13 And we will have another Federal Register notice
14 and another comment period. You will probably be
15 hearing about that in a lot of different ways.
16 And we hope that you will expand on that.

17 But one of our key takeaways that I have and
18 that we hope is present in the documents -- and if
19 not, let us know -- there's not just one approach.
20 This is not just about patient-reported outcomes
21 and that we want a lot of people to be involved
22 and we hope that you will send us your examples

1 and your practices so that we can include them as
2 well.

3 Unless my FDA colleagues have other comments
4 or thoughts? All right. Thank you very much and
5 have a great day.

6 (Applause.)

7

8 (Whereupon, the meeting was concluded at 4:26
9 p.m.)

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CERTIFICATE OF NOTARY PUBLIC

I, IRENE GRAY, the officer before whom the foregoing proceeding was taken, do hereby certify that the proceedings were recorded by me and thereafter reduced to typewriting under my direction; that said proceedings are a true and accurate record to the best of my knowledge, skills, and ability; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this was taken; and, further, that I am not a relative or employee of any counsel or attorney employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.



IRENE GRAY

Notary Public in and for the

State of Maryland

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CERTIFICATE OF TRANSCRIBER

I, BENJAMIN GRAHAM, do hereby certify that
this transcript was prepared from audio to the
best of my ability.

I am neither counsel for, related to, nor
employed by any of the parties to this action, nor
financially or otherwise interested in the outcome
of this action.



12/27/2017

DATE

BENJAMIN GRAHAM

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