U.S. FOOD & DRUG ADMINISTRATION

Patient-Focused Drug Development

COLLECTING COMPREHENSIVE AND REPRESENTATIVE INPUT

December 18, 2017

WELCOME

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Today's Workshop Sessions

- Patient-Focused Drug Development: Defining Key Terminology
- Overview of FDA's Approach to PFDD Guidance 1
- Session I: Defining Research Objectives and Methodological Considerations for Designing Studies to Collect Patient Experience Data
    - Lunch
- Session II: Methodological Considerations for Data Collection, Analysis and Operationalization
- Session III: Translating Best Practice into Real Practice - Developing Guiding Examples
- Session IV: Identifying Key Themes and Next Steps
- Open Public Comment
- Closing Remarks

OPENING REMARKS

Theresa Mullin, PhD
Director
Office of Strategic Programs
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Background

- FDA initiated **Patient Focused Drug Development (PFDD)**
  - and conducted over 20 meetings under PDUFA V (2012-2017) to directly obtain patients' point of view on the severity of their condition, its impact on daily life, and their assessments of available treatment options
- Key learnings:
  - Patients are experts on what it is like to live with their condition
  - Their "chief complaints" may not be factored explicitly into drug development plans, including measures of drug benefit planned in trials
- Our next steps:
  - Engage community to discuss approaches that:
    - Bridge from PFDD meetings to more systematic collection
    - Generate meaningful input on patients' experiences and perspectives to inform drug development and benefit-risk assessment
    - Are methodologically sound and "fit for purpose" in drug development and regulatory context
  - Issue guidance

PDUFA VI: Incorporation of Patient's Voice in Drug Development and Decision-Making

Conduct public workshops and develop series of guidance documents on:

1. **Collecting comprehensive patient community input on burden of disease and current therapy (FY 2018)**
2. Development of holistic set of impacts (e.g., burden of disease and burden of treatment) most important to patients (FY 2019)
3. Identifying and developing good measures for the identified set of impacts that can then be used in clinical trials. (FY 2020)
4. Incorporating measures (COAs) into endpoints considered significantly robust for regulatory decision making (FY 2021)

https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM511438.pdf

21st Century Cures Act, Title III Subtitle A
Patient Focused Drug Development Section 3002

(a) PUBLICATION OF GUIDANCE DOCUMENTS. Secretary shall… issue draft and final versions of one or more guidance documents, over a period of 5 years, regarding the collection of patient experience data, and the use of such data and related information in drug development. CONTENTS.—The guidance documents described in subsection (a) shall address—

(1) methodological approaches that a person seeking to collect patient experience data for submission to, and proposed use by, the Secretary in regulatory decision making may use, that are relevant and objective and ensure that such data are accurate and representative of the intended population, including methods to collect meaningful patient input throughout the drug development process and methodological considerations for data collection, reporting, management, and analysis;

(2) methodological approaches that may be used to develop and identify what is most important to patients with respect to burden of disease, burden of treatment, and the benefits and risks in the management of the patient's disease;

(3) approaches to identifying and developing methods to measure impacts to patients that will help facilitate collection of patient experience data in clinical trials;

(4) methodologies, standards, and technologies to collect and analyze clinical outcome assessments for purposes of regulatory decision making;

21st Century Cures Act, Title III Subtitle A
Patient Focused Drug Development Section 3002

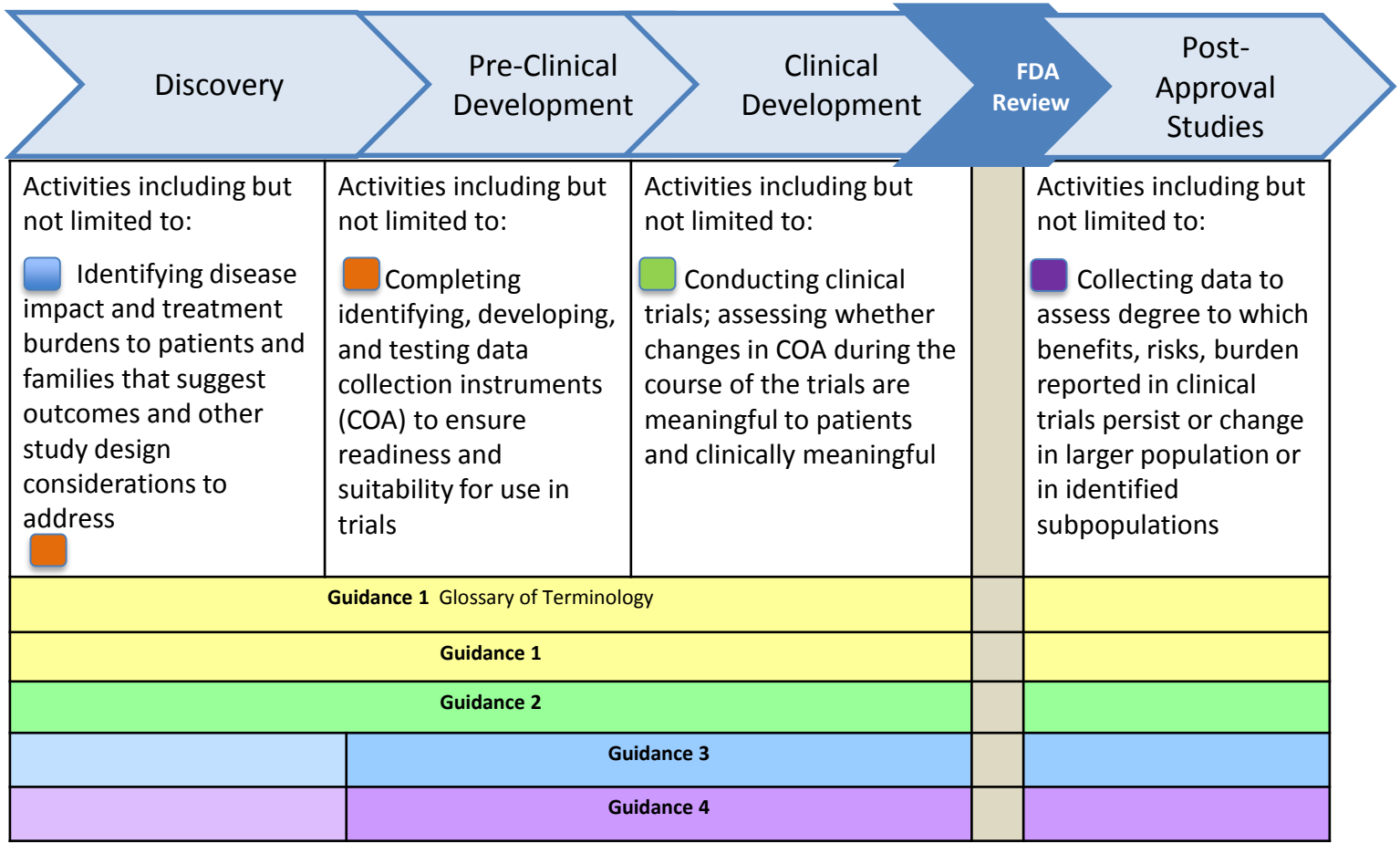
PUBLICATION OF GUIDANCE DOCUMENTS – CONTENTS *(cont.)*

(5) how a person seeking to develop and submit proposed draft guidance relating to patient experience data for consideration by the Secretary may submit such proposed draft guidance to the Secretary;

(6) the format and content required for submissions under this section to the Secretary, including with respect to the information described in paragraph (1);

(7) how the Secretary intends to respond to submissions of information described in paragraph (1), if applicable, including any timeframe for response when such submission is not part of a regulatory application or other submission that has an associated timeframe for response; and

(8) how the Secretary, if appropriate, anticipates using relevant patient experience data and related information, including with respect to the structured risk-benefit assessment framework described in section 505(d) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(d)), to inform regulatory decision making.


Discovery
Pre-Clinical Development
Clinical Development
FDA Review
Post-Approval Studies
Activities including but not limited to:
Identifying disease impact and treatment burdens to patients and families that suggest outcomes and other study design considerations to address
Activities including but not limited to:
Completing identifying, developing, and testing data collection instruments (COA) to ensure readiness and suitability for use in trials
Activities including but not limited to:
Conducting clinical trials; assessing whether changes in COA during the course of the trials are meaningful to patients and clinically meaningful
Activities including but not limited to:
Collecting data to assess degree to which benefits, risks, burden reported in clinical trials persist or change in larger population or in identified subpopulations
Guidance 1 Glossary of Terminology
Guidance 1
Guidance 2
Guidance 3
Guidance 4

Questions for Today for You

- We published a Guidance 1 Discussion Document to help focus discussion and get your input, in particular:
  1. What level of detail do you think is appropriate for this FDA guidance series?
  2. What document structure and content would be most useful for this first guidance?
  3. Does this document make clear that we understand that many potential research methods are available and not all could be included in the document; that FDA is open to discussion of the methods described and other methods, both within medical product programs and in the pre-competitive space?
  4. What are the most important time points when FDA input could be maximally helpful?
  5. The PDUFA VI commitment letter calls for a glossary of standardized nomenclature and terminology relevant to all four guidance documents.
     - Are the proposed draft definitions within the glossary clear and do they serve to facilitate dialogue?

PATIENT-FOCUSED DRUG DEVELOPMENT: DEFINING KEY TERMINOLOGY

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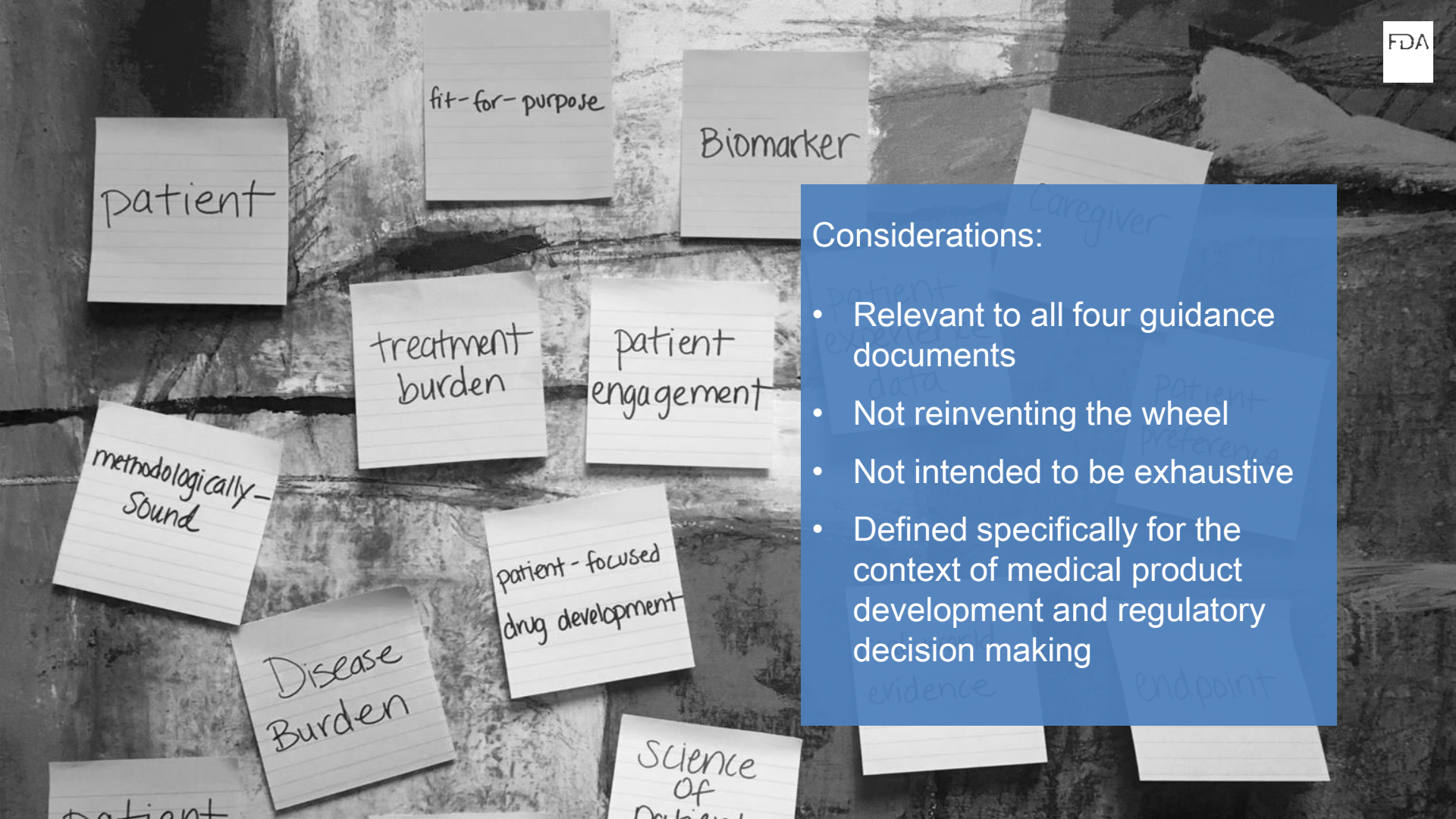
The goal of this glossary is to provide

standardized nomenclature and terminologies related to patient-focused medical product development.



Considerations:

- Relevant to all four guidance documents
- Not reinventing the wheel
- Not intended to be exhaustive
- Defined specifically for the context of medical product development and regulatory decision making

Overview of Development Process

1. Identification of terms

- Literature review and outline of guidance series' topics

2. Curation of existing definitions

- Federal resources, literature review, external resources

3. Small-group facilitated discussion

- 4 small groups, each with CBER, CDER, & CDRH experts
- Each group had a set of terms and if applicable, existing definitions, and were asked to discuss and define
- Followed by opportunity to seek feedback from other FDA colleagues

4. Large-group facilitated discussion

- Focused on reaching consensus for overarching PFDD terms – definitions, as well as relationships between terms, e.g., hierarchy, related terms, etc.

Putting it all together

The **OUTCOME:** Patient-focused Drug Development, also referred to as Patient-Focused Medical Product Development

The **WHO**:

- Patient, Caregiver, Patient Representative, Patient Advocate

The **WHAT**:

- Perspectives, preferences, experiences
- Evidence: patient experience data, patient input, patient-reported outcome (PRO), patient perspective, patient preference information

The **HOW**

- Patient engagement, patient preference method, science of patient input

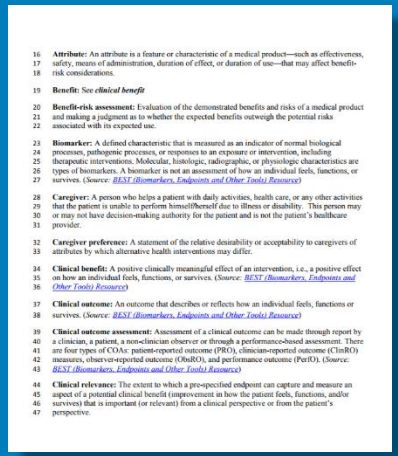
The **HOW WELL**

- Fit-for-purpose, methodologically-sound, representativeness

*Only terms from draft glossary listed here, not intended to be comprehensive

This glossary will be a **living document.**

FDA will post the glossary on its public website, so that it can be updated periodically.



Attribute: An attribute is a feature or characteristic of a medical product—such as effectiveness, safety, means of administration, duration of effect, or duration of use—that may affect benefit-risk considerations.

Benefit: See ***clinical benefit***

Benefit-risk assessment: Evaluation of the demonstrated benefits and risks of a medical product and making a judgment as to whether the expected benefits outweigh the potential risks associated with its expected use.

Biomarker: A defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions. Molecular, histologic, radiographic, or physiologic characteristics are types of biomarkers. A biomarker is not an assessment of how an individual feels, functions, or survives. (*Source:* *BEST (Biomarkers, Endpoints and Other Tools) Resource*)

Caregiver: A person who helps a patient with daily activities, health care, or any other activities that the patient is unable to perform himself/herself due to illness or disability. This person may or may not have decision-making authority for the patient and is not the patient's healthcare provider.

Caregiver preference: A statement of the relative desirability or acceptability to caregivers of attributes by which alternative health interventions may differ.

Clinical benefit: A positive clinically meaningful effect of an intervention, i.e., a positive effect on how an individual feels, functions, or survives. (*Source:* *BEST (Biomarkers, Endpoints and Other Tools) Resource*)

Clinical outcome: An outcome that describes or reflects how an individual feels, functions or survives. (*Source:* *BEST (Biomarkers, Endpoints and Other Tools) Resource*)

Clinical outcome assessment: Assessment of a clinical outcome can be made through report by a clinician, a patient, a non-clinician observer or through a performance-based assessment. There are four types of COAs: patient-reported outcome (PRO), clinician-reported outcome (ClinRO) measures, observer-reported outcome (ObsRO), and performance outcome (PerfO). (*Source:* *BEST (Biomarkers, Endpoints and Other Tools) Resource*)

Clinical relevance: The extent to which a pre-specified endpoint can capture and measure an aspect of a potential clinical benefit (improvement in how the patient feels, functions, and/or survives) that is important (or relevant) from a clinical perspective or from the patient's perspective.

Please provide us with feedback through the public docket:

- Keeping the scope of the glossary in mind, are any terms missing?
- Are the definitions clear and understandable?
- Public docket: https://www.regulations.gov/docket?D=FDA-2017-N-5896
- The public docket will close on February 16, 2018.

OVERVIEW OF FDA'S APPROACH TO PFDD GUIDANCE 1

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Our Ultimate Purpose: Understand Patients' Perspectives on Benefits and Risks

- **Clinical benefit**: A ***positive clinically meaningful effect*** of an intervention, i.e., a positive effect on how an individual ***feels***, ***functions***, or ***survives***
  - How long a patient lives
  - How a patient feels or functions in daily life (includes both improvement as well as prevention/slowing decline)
- **Clinical outcome:** An outcome that describes or reflects how an individual feels, functions or survives
  - Assessed using clinical outcome assessments (COAs)
- Careful assessment of patients' views on benefits and risks are an important part of regulatory decision-making

What is patient experience data?

- Data that are collected by any persons and are intended to provide information about patients' experiences with a disease or condition
- Includes the experiences, perspectives, needs and priorities of patients related to (but not limited to)
  1) Symptoms of their condition and its natural history
  2) Impact of the conditions on their functioning and quality of life
  3) Experience with treatments
  4) Input on which outcomes are important to them
  5) Patient preferences for outcomes and treatments
  6) Relative importance of any issue as defined by patients

Source: Title III, Section 3002(c) of the 21st Century Cures Act

Why is it important to collect patient experience data?

- Patients are experts in their own experience of their disease or condition and the ultimate consumers of medical products
- Patient experience data can inform medical product development and enhance regulatory decision making to address patients' needs

Where does patient experience data come from?

- The patient's journey should be defined from the patient perspective (where possible) informed by input from patient partners and clinicians

Types of Patient Partners

- A **patient** is any individual with or at risk of a specific health condition, whether or not they currently receive any therapy to prevent or treat that condition. Patients are the individuals who directly experience the benefits and harms associated with medical products.

- A **caregiver** is a person who helps a patient with daily activities, health care, or any other activities that the patient is unable to perform himself/herself due to illness or disability. This person may or may not have decision-making authority for the patient and is not the patient's healthcare provider.

- A **patient advocacy group** is a group of individuals who may or may not be part of the target patient population, who have a role in promoting an interest or cause to influence policy with respect to patients' health or healthcare.

When do you collect patient experience data?

- Before and throughout the medical product development process
- Precompetitive collaboration is encouraged!

Who can collect and submit patient experience data?

- Anyone can collect and submit patient experience data, including
  - Patients
  - Family members and caregivers of patients
  - Patient advocacy organizations
  - Disease research foundations
  - Researchers
  - Drug manufacturers

How can external stakeholders submit patient experience data to FDA?

- Various pathways exist
- FDA guidance on how to submit patient experience data is under development
- Depending on the purpose and type of data, different content and formats may be appropriate

How is patient experience data used for regulatory purposes?

- Patient experience data is used to inform
  - Clinical trial design
  - Trial endpoint development and selection
  - Regulatory reviews including benefit-risk assessments

How do you collect patient experience data?

- FDA recommends qualitative, quantitative or mixed methods (use of both qualitative and quantitative methods) to collect robust and meaningful patient experience data

PDUFA VI: Incorporation of Patient's Voice in Drug Development and Decision-Making

Conduct public workshops and develop series of guidance documents on

1. **Collecting comprehensive patient community input on burden of disease and current therapy (FY 2018)**
   - ***Who do you ask? Who do you get input from? Why? How do you collect it?***
2. Development of holistic set of impacts (e.g., burden of disease and burden of treatment) most important to patients (FY 2019)
   - *What do you ask? Why? How do you ask non-leading questions that are well understood by a wide range of patients and others? Methods to avoid misleading results*
3. Deciding what to measure in a clinical trial (FY 2020)
   - *How will you select what to measure in a clinical trial? Refining the set of impacts to what is measurable and likely to show clinical benefit in a specific treatment trial.*
4. Identifying and developing good measures for the identified set of impacts and incorporating measures (COAs) into endpoints considered significantly robust for regulatory decision making (FY 2021)
   - *What is the right endpoint? How to use the selected tool in a trial?*

https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM511438.pdf

Guidance 1: Purpose

- To present methods for collecting information on the patient experience that is representative of the intended population

- To present a synopsis of methods on how to operationalize and standardize data collection, analysis, and dissemination of patient experience data

Guidance 1: Approach

- Intended for a broad audience to serve as a focus for discussion among FDA with multiple stakeholder groups
- Intended to encourage patient involvement as partners before and throughout the medical product development process
- Intended to promote a collaborative process in the collection of robust patient experience data
- Emphasizes the concept of fit-for-purpose (i.e., tools matched to the specific research questions and regulatory needs)
- Recognizes that the science of patient input is an evolving field
- Recommends a pragmatic step-wise approach to provide usable patient experience information to FDA

Does Guidance 1 Address COAs or Patient Preference Information?

- Provides a framework for collecting representative patient input that can be used to inform COAs and patient preference information (PPI)
- Does not cover collecting and analyzing COA or PPI data
- Some of those issues are addressed in the following guidance for industry
  - *Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims*
  - *Patient Preference Information—Voluntary Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and De Novo Requests, and Inclusion in Decision Summaries and Device Labeling*

Overview of Guidance 1 Workshop Discussion Document

- General Considerations for Collecting Patient Experience Data
  - Defining the research objectives and questions
  - From whom to collect information
  - Determining the study design and research setting
  - Constructing a sampling frame
  - Additional considerations to achieve sufficient representation
- Methods for Collecting & Analyzing Data
- Operationalizing and Standardizing Data Collection & Data Management

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

Michelle Campbell, PhD
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Session 1:
Defining Research Objectives and Methodological Considerations Designing Studies to Collect Patient Experience Data

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U.S. Food and Drug Administration

General Considerations for Collecting Patient Experience Data

Methods for Collecting & Analyzing Data

Operationalizing and Standardizing Data Collection & Data Management

Overview

- **Factors to consider when selecting a research approach**

What are the **research goals or research questions** to be addressed?

What is the **target population**?

What is the **availability** of people in that population?

Type of **information** you **need to generate** through the study

Short-term and long-term impacts of the information gathered through the study

What **type of information is most valuable** to achieve these goals?

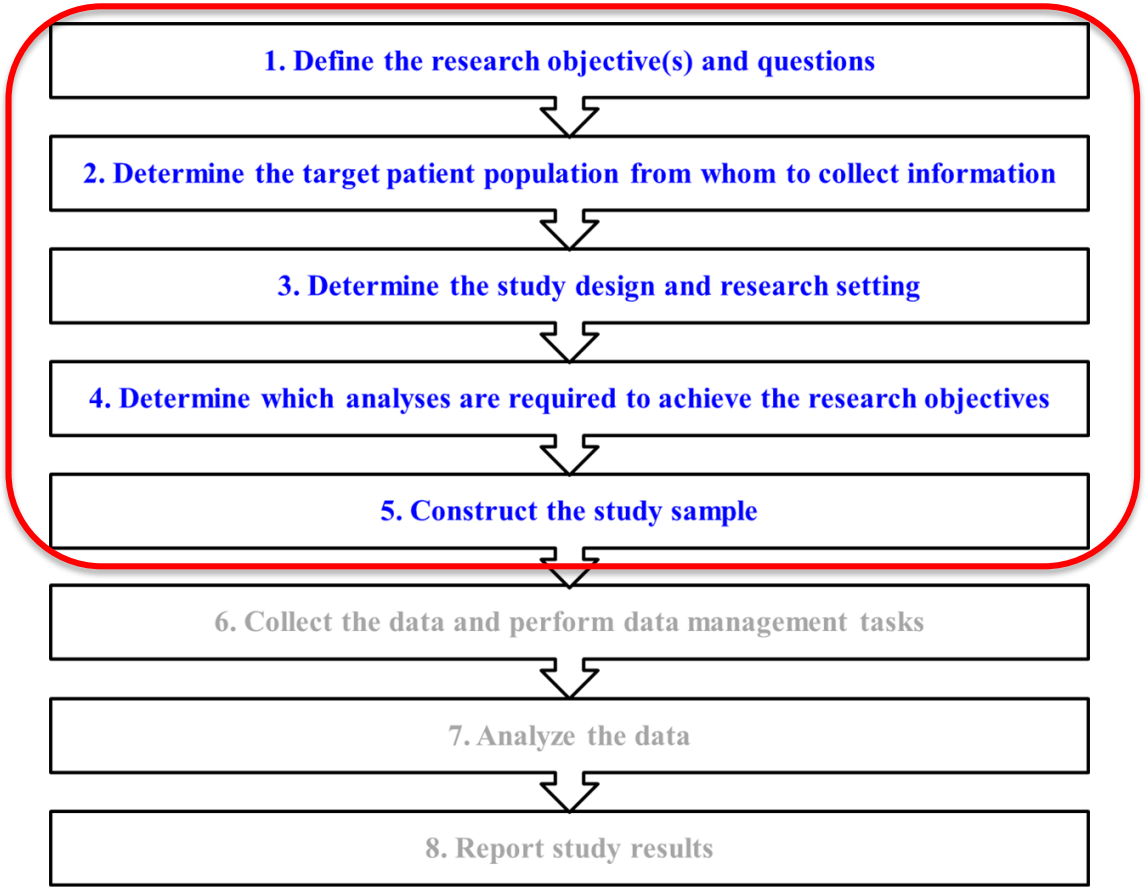
What is the **expected impact of the information** you intend to gather from your research?

Amount of time you have to conduct your studies

Study **budget** (including staffing, travel time, facilities costs, remuneration, data storage, management, and analysis)

Source: Johnson and Christensen 2017; Teherani, Martimianakis, et al. 2015

General Steps for Conducting Studies



General Considerations

Defining Research Objectives and Questions

- Research objectives should be specific and defined by research questions
- Research objectives and questions should inform which methodological approaches you decide to use in your research
- Consult the following when drafting research questions and objectives:
  - Published and unpublished literature
  - Expert consultation

General Considerations

Defining Research Objectives and Questions

Example:

Research objective: To explore the attitudes and needs of patients with human immunodeficiency virus (HIV)

Research questions:

1. How does HIV impact patients' daily lives?
2. Why might HIV patients not accept treatment?
3. What do patients look for in an ideal treatment for HIV?

Next steps: After defining your research objective and questions, you can start thinking about what research method to choose to meet your goal. If patients feel uncomfortable asking questions or sharing concerns about living with HIV, it might be more suitable to engage them in one-on-one interviews over the telephone to provide them with a more comfortable interview setting rather than in group discussions or even administering a survey.

General Considerations

Whom to Collect Information From

- **Define the target population**

Example: If you wish to understand the views and preferences of all individuals with Parkinson's disease (PD) in the world, then the target population could be defined as the set of all individuals who have been diagnosed with PD. If you are interested in a subset of PD patients, such as patients diagnosed within the last 5 years, then the target patient population could be restricted accordingly. The target population may also be restricted to a certain geographic area, such as PD patients in the US or the state of California.

General Considerations

Whom to Collect Information From

- Determine who would be the best source of information regarding the patient experience
  - The reporter (e.g., patient, caregiver, clinician)

- Factors to consider when determining if self-report is feasible:
  - Age
  - Level of cognitive development
  - Communication skills
  - Health literacy
  - Insight
  - Health state
  - Co-morbidities

General Considerations

Whom to Collect Information From

Example: If you are studying asthma in patients aged 4-17 years old, then the reporter might be (a) the patient's primary caregiver or parent for young children who cannot provide a reliable response and (b) the patient themselves (if determined they are of age to provide a reliable response).

General Considerations

Whom to Collect Information From

- Pre-specify subgroups of interest at study design phase
- Recommended Considerations:
  - Number of subgroups being proposed for analysis and inference.
  - Reporter type (e.g., patients versus primary caregivers)
  - Reporter characteristics (e.g., socioeconomic, demographic, cultural, linguistic, clinical, or other factors pertinent to the disease/condition)
  - Prevalent symptoms (for diseases/conditions with notable symptom heterogeneity)

Design/Research Setting – Representative Input

Guidance 1: framework for collecting patient experience data that are not only comprehensive but also **representative** of the underlying target population.

Design/Research Setting – Representative Input

What is representativeness?

- Cannot study entire target population
- Two ways of thinking about representativeness:
  - Generalizability
  - Representation
- Depends on your research objectives

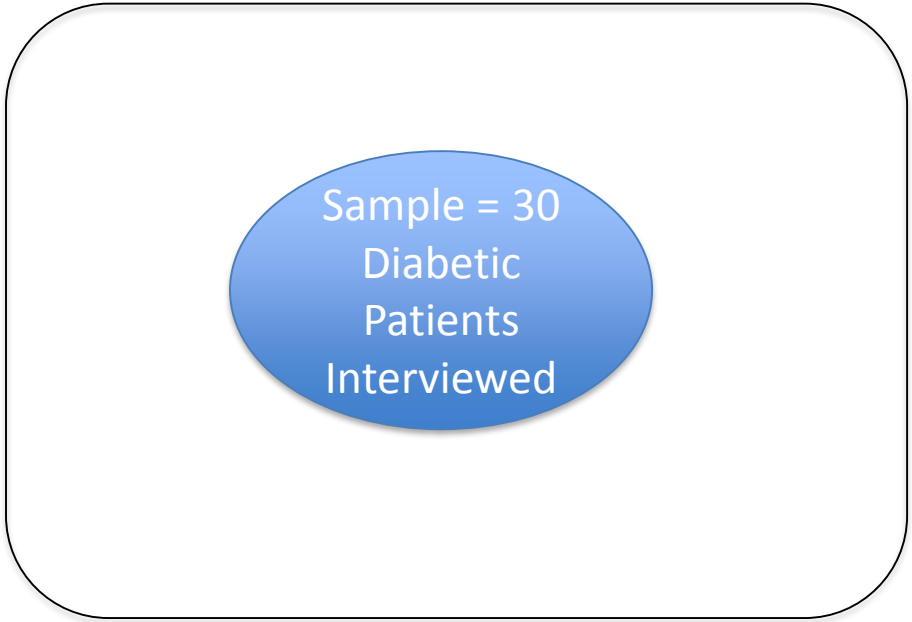
Design/Research Setting – Representative Input

Generalizability:

Statements made about patient experience based on your study sample is generalizable to your target population.

Design/Research Setting – Representative Input

Target Population = All Diabetic Patients in US



Design/Research Setting – Representative Input

Representation:

Patients in the study sample reflect the diversity/heterogeneity of patient characteristics in the target population but the distribution of these characteristics in the sample could be very different from those in the population.

For example, the sample of 30 diabetic patients consists of similar numbers of Blacks, Whites, Asians and of similar proportions of young and old.

Design/Research Setting – Generalizability

- Getting there: Probability/Random sampling
  - Simple random sampling (SRS)
  - Stratified SRS
  - Cluster sampling
  - Multi-stage probability sampling
  - Other variations
- Document does not discuss sampling schemes
- References literature for detail coverage

Design/Research Setting – Generalizability

- Selection probabilities ***known***
- Information in sample weighted by selection probabilities
- Weighting enables generalizability to target population.

Design/Research Setting – Representation

- Non-probability/non-random sampling:
  - Convenience
  - Purposive
  - Quota
  - Others
- Selection mechanism not quantifiable
- Generalizability unknown

Design/Research Setting – Sample Size

How you calculate sample size depends on:

- Research objective
- Types of endpoints (categorical/continuous/longitudinal)
- Study design (survey, clinical trial, observational)
- Method of analysis (exact, large sample, regression)
- Operating characteristics (power, false positives, precision)
- Assessment of subgroups

Sampling Frame

- List members of target population: disease registry
- Ideally, should be near complete
- Facilitates implementation of probability sampling
- Not always readily available
- Need to create

Representation: Additional Considerations

- Age, sex, race, education
- Cultural background
- Reading, writing, speaking abilities
- Disease severity and subtypes
- Physical/cognitive abilities

Key Takeaways

- Clear research goals/questions
- Clearly-defined target population
- Type of information you need to answer your questions
- Who will provide the information you need
- How you will achieve representativeness
- How many people to include in your study

Session I: Panel Discussion

- Kunthel By, FDA
- Steve Cohen, RTI International
- Ebony Dashiell-Aje, FDA
- Richard Gershon, Northwestern University
- Meena Khare, CDC
- Liz Piault-Louis, Genentech
- Suzanne Vernon, Bateman Horne Center

Session I: Panel Discussion

Objective: Discuss general considerations for collecting patient experience data. Explore factors and approaches to ensure that the patient input to be collected is sufficiently representative of the range of clinically relevant diversity in the patient population.

Questions to address:

- Are there are any other factors to consider when defining research objectives and designing studies to collect patient experience data that should be included in the guidance?
- What are other factors and/or approaches to consider to ensure collection of representative input from the target population (patients with disease of interest)?
- In which situations is it more important to sample patients using a probability-based method? In which situations is it less important? What will be gained and what may be lost?

LUNCH

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

Scott Komo, PhD
Office of Biostatistics
Office of Translational Sciences
Center for Drug Evaluation and Research
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Session 2:
Methodological Considerations for Data Collection, Analysis and Operationalization

Selena Daniels, PharmD, MS
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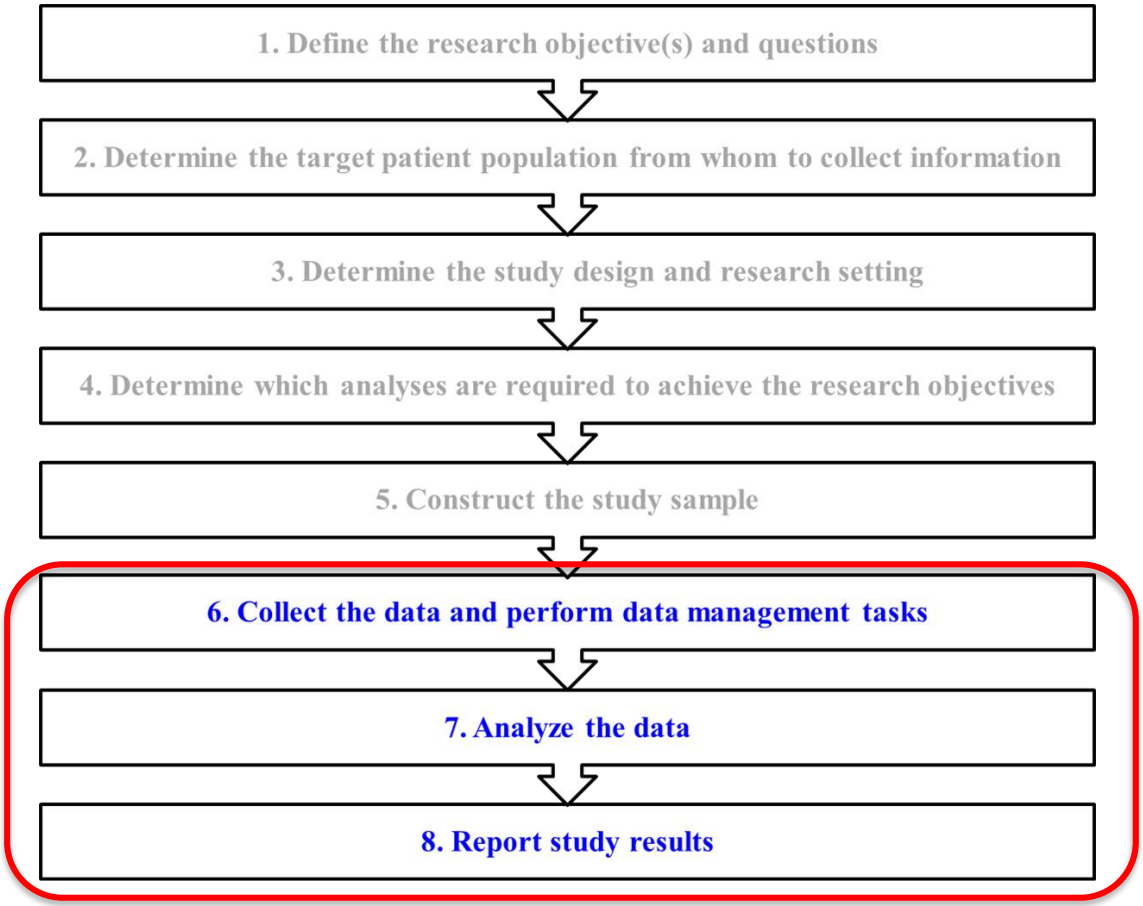
General Steps for Conducting Studies



General Considerations for Collecting Patient Experience Data

Methods for Collecting & Analyzing Data

Operationalizing and Standardizing Data Collection & Data Management

Methods for Collecting Data

	Qualitative Methods	Quantitative Methods	Mixed Methods
Method	Uses direct communication to explore or confirm the meaning of interpretation of a topic from the participant's perspective	Uses a tool (survey or questionnaire) that provides numerical information	Uses both qualitative and quantitative data and approaches in an integrated manner in the same study or a set of related studies
Scientific Question*	*What aspects of disease are important to patients for measurement and reporting of clinical trial results?*	*How do we design a questionnaire measuring aspects of disease?*	*Do we measure symptom severity or frequency?*

***Example questions**

Source: Adapted from Teddlie & Tashakkori (2009)

How to Determine which Method to Use?

FDA

METHODS

QUALITATIVE | QUANTITATIVE | MIXED

- Research Question/Goals
- Method Characteristics
- Target Population
- Expected Data

Qualitative Methods

Key Outcomes

- ***Discover***, rather than test, variables
- Determine the meaning of and refine specific research concepts

Sources

- Interviews (one-on-one interviews, focus groups, social media, etc.)
- Consensus panels

Analysis

- General steps:

Compile & Organize data → Classify data → Interpret data → Represent & Visualize data

Quantitative Methods

Key Outcomes

- ***Test***, rather than, discover variables

Sources

- Tool (survey or questionnaire)

Analysis

- Analytic approach should be appropriate for the:

  Research objectives Study design Data type

Mixed Methods

Key Outcomes

- ***Discover*** and/or ***test*** variables

Sources

- Interviews (one-on-one interviews, focus groups, social media, etc.)
- Consensus panels
- Tools (surveys or questionnaires)

Analysis

- Combination of analyses for qualitative and quantitative methods

General Considerations for Collecting Patient Experience Data

Methods for Collecting & Analyzing Data

Operationalizing and Standardizing Data Collection & Data Management

Operationalizing & Standardizing

Locating Patients/Sites

Identify appropriate sample and/or sites to study

Gaining Access

Seek permission from a human subjects review board prior to study and comply with the institutional review board (IRB)

Data Management & Storage

Formulate data management and storage plan

Sampling

Determine strategy for the sampling of patients or sites

Resolving Site/Field Issues

Provide standardized training to research team members

Collecting Data

Consider the most appropriate data collection approach for research objective

Recording Info

Develop written forms or protocols to collect data

Operationalizing & Standardizing

Submission Materials to FDA

- Detailed documentation of patient experience studies including but not limited to:

  ❑ **Study protocols**
  - Interview or Discussion guide, if applicable
  - Tools (surveys or questionnaires)

  ❑ **Study reports**
  - Transcripts, if applicable and available

Additional Information

Appendix 1
Timelines for Development of Guidances

Appendix 2
Standards & Requirements Pertaining to Submission of Data

Appendix 3
Qualitative Interview Question Framing: Best Practices

Appendix 4
Delphi Panel Techniques & Characteristics

Appendix 5
Considerations for Data Management

Appendix 6
Methods for Collecting Patient Experience Data

Key Takeaways

- Research objective/questions should inform the methodological approach used to conduct research
  - *Other factors to consider are*: characteristics of method, target population, and expected data

- Data collection process (including data quality issues) and reporting of findings should be standardized to the extent possible

Session II: Panel Discussion

- Steve Cohen, RTI International
- Selena Daniels, FDA
- Sheri Fehnel, RTI Health Solutions
- Gary Globe, Amgen
- Isabelle Lousada, Amyloidosis Research Consortium
- Kai Ruggeri, Columbia University

Session II: Panel Discussion

Objective: Explore methods to consider at an early stage in drug development to gain a thorough account of patients' experience and perspectives on their disease and available therapy. Discuss approaches to consider for collecting, analyzing, managing, and reporting the information.

Questions to address:

- Future guidances will discuss in more detail qualitative, quantitative, and mixed methods. Is more detail (or less) needed in this first guidance about which source (e.g., interviews, focus groups, consensus panel, etc.) to use to collect data? Is anything missing? Include in your comments feedback on the information in the appendices as well.
- Similar question about operationalizing and standardizing data collection and data management. Is more detail (or less) needed in this first guidance? Is anything missing?
- Are there any other factors to consider regarding the selection of methods to collect and analyze patient experience data that should be included in the guidance?
- Are there any other factors to consider regarding the operationalization of the data collection process?

SESSION III: TRANSLATING BEST PRACTICES INTO REAL PRACTICE – DEVELOPING GUIDING EXAMPLES

Sara Eggers, PhD
Decision Support and Analysis Team
Office of Program and Strategic Analysis/Office of Strategic Programs
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

Megan Moncur, MS
Office of Biostatistics and Epidemiology
Center for Biologics Evaluation and Research
U.S. Food and Drug Administration

Session III: Panel Discussion

- Richard Gershon, Northwestern University
- Telba Irony, FDA
- Susan McCune, FDA
- April Naegeli, Eli Lilly
- Sally Okun, PatientsLikeMe
- Elizabeth Stuart, Johns Hopkins University

List of Examples from the Discussion Document

	Example & concept illustrated	Page #
1.	Defining research objectives and questions in human immunodeficiency virus (HIV)	15
2.	Defining the target population in Parkinson's disease (PD)	15
3.	Determining the reporter (i.e. who will provide the information) in asthma (age 14-17)	16
4.	Probability sampling in PD	20
5.	Sample size calculation for efficacy superiority clinical trial	21
6.	Constructing a sampling frame – accessing your target population via a sample of physicians (identified through physician listing resources)	22
7.	Quantitative research methods – Psoriasis Symptom Questionnaire	27
8.	Mixed methods research – diabetes survey	27
9.	Data collection methods – advantages and disadvantages of a study consisting only of interviews	30

Session III: Panel Discussion

Objective: Identify common challenges in collecting patient experience data and explore ways to avoid these challenges and maximize success. Discuss situations where things did not go as planned, and situations where things did go well. Information from this panel session will inform the development of case studies or vignettes to help support important aspects of the draft guidance.

Questions to address:

- What are your thoughts on the examples that are currently included in the discussion document?
- What concepts from the discussion document would be helpful to illustrate through examples or case studies?
- When collecting patient experience data, what are some common challenges seen in study design or implementation that might be useful to address through additional examples? How can that challenge result in data that are less suitable for regulatory purposes? What are practical ways to avoid the challenge?
- Are there novel approaches or exemplars for collecting patient experience data that could be useful examples? How could someone replicate the effort?

Scenario A

(Hypothetical situation, for discussion purposes only)

Situation

- Researchers used a probability sampling scheme to send out surveys to patients.
- The researchers note that the response rate is low.
- The submitted report includes only the results and demographics of the responders. It does not include demographic information on the non-responders.

Potential Regulatory Concern

- Low response rates raise questions about the representativeness of the study participants to the target patient population and the risk of non-response bias.
- Patients who respond may systematically differ from people who do not respond.
- Due to high non-response, you end up with a non-probability sample, unless appropriate weighting adjusted for non-response is employed.

Practical Solution to Enhance the Research Effort

- Take efforts to increase participation rates (e.g., minimize survey burden, plan for follow-up).
- Include a pre-specified analysis plan that incorporates weights derived from the sampling scheme as well as weights for possible high non-response. Update this plan as needed.
- You may consider modifying your sampling approach to address non-response.

BREAK

SESSION IV: IDENTIFYING KEY THEMES AND NEXT STEPS

Sara Eggers, PhD
Decision Support and Analysis Team
Office of Program and Strategic Analysis/Office of Strategic Programs
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

Session IV: Panel Discussion

- Conny Berlin, Novartis
- Sonya Eremenco, Critical Path Institute
- Kimberly McCleary, FasterCures
- Theresa Mullin, FDA
- Elektra Papadopoulos, FDA
- Celia Witten, FDA

Session IV: Panel Discussion

Objective: Reflect on the day's discussion, specifically any themes that emerged throughout the day. Discuss key considerations that should guide FDA's completion of the first in the series of PFDD guidances.

Questions to address:

- What are the three most important messages you have taken away from the workshop discussion that should guide FDA as we complete this draft guidance?
- How can FDA strike the right balance to meet stakeholders' needs? How well do the discussion documents for today's meeting strike this balance?
- Would the overall structure and format of the discussion documents for today's meeting be reasonable for the guidance? Do you have additional structure and format recommendations for FDA to consider when developing the draft guidance?
- Considering that this is a first in a series of guidances that will be developed over time, how might FDA best facilitate stakeholders' understanding of the big picture and how all the pieces fit together?

OPEN PUBLIC COMMENT

CLOSING REMARKS

Laura Lee Johnson, PhD
Acting Director, Division of Biometrics III
Office of Biostatistics
Office of Translational Sciences
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

PRAGMATIC
FEASIBLE
USER-FRIENDLY

Questions for You

1. Level of detail
   - Balance of level of detail and comprehensiveness
   - If an additional layer of detail would be useful please discuss what that should be and how to present it
2. Document structure for this first guidance
3. Missing content that could be useful for this first guidance? Corrections to provided content?
4. Is it clear FDA is open to discussion of the methods described and other methods?

Questions for You

5. The PDUFA VI commitment letter calls for a glossary of standardized nomenclature and terminology relevant to all four guidance documents
   - Are proposed draft definitions clear?
   - Do they serve to facilitate dialogue?

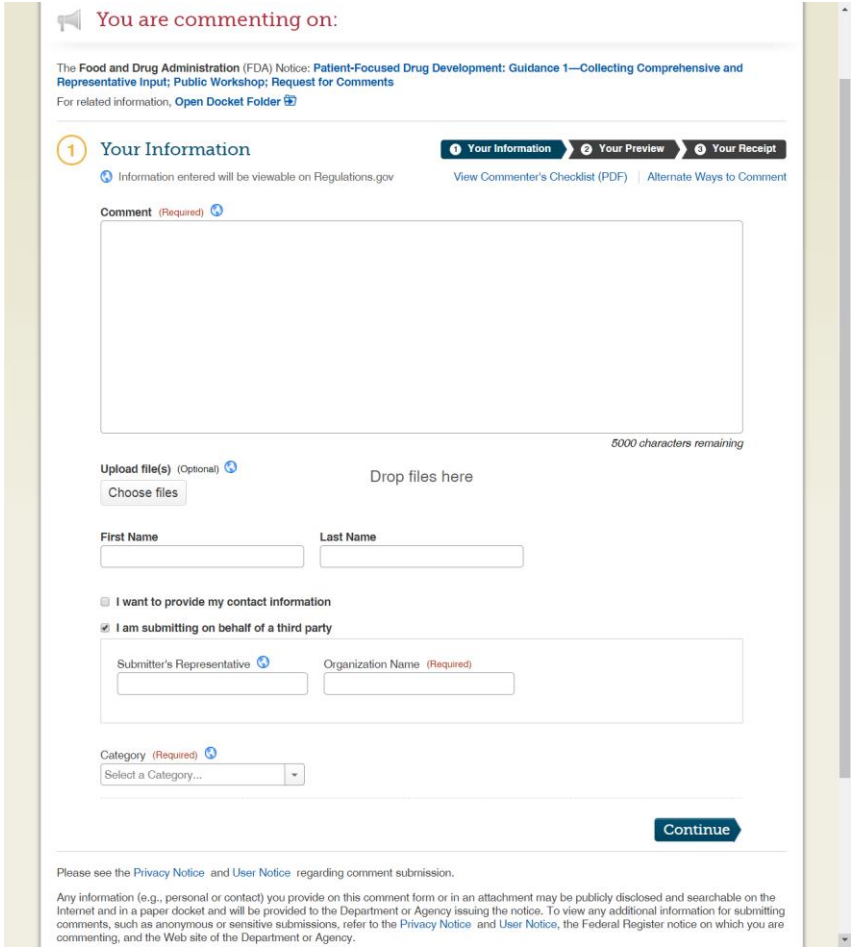
Questions for You

6. Most important time points when FDA input could be maximally helpful
7. Additional external resources to consider

If you have information, documents, thoughts, comments, or anything else to share, please submit (quickly) to the public docket for this meeting!

How to Add Comments to the Docket for this Workshop

- Go to https://www.regulations.gov/docket?D=FDA-2017-N-5896
- Comments due Friday, February 16, 2018 (11:59pm ET)
  - Please submit comments as soon as possible, preferably in the next few weeks
- Need to publish draft guidance June 2018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The Food and Drug Administration (FDA) Notice: Patient-Focused Drug Development: Guidance 1—Collecting Comprehensive and Representative Input; Public Workshop; Request for Comments
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Draft Guidance 1

- Expected June 2018
- Federal Register Notice and comment period

Thank you for participating in today's workshop!

Please submit your comments to the docket for this meeting

https://www.regulations.gov/docket?D=FDA-2017-N-5896


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