U.S. FOOD & DRUG ADMINISTRATION

PATIENT-FOCUSED DRUG DEVELOPMENT
PUBLIC WORKSHOP ON GUIDANCE 1

COLLECTING COMPREHENSIVE AND REPRESENTATIVE INPUT

DISCUSSION DOCUMENT

Workshop Date: December 18, 2017

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1. INTRODUCTION AND BACKGROUND

This and future discussion documents are intended to provide a basis for discussion that will inform the development of guidance documents to facilitate collection and submission of usable patient experience data for medical product development and regulatory decision making. This document, its appendices, and the draft glossary provide background for the FDA public workshop, "Patient-Focused Drug Development: Guidance 1 – Collecting Comprehensive and Representative Input," on December 18, 2017.

FDA will develop a series of four guidance documents describing in a stepwise manner how stakeholders can collect and submit information from patients and caregivers to be used for medical product development and regulatory decision making. These four guidance documents will focus on practical approaches and methods to collect and utilize robust and meaningful patient and caregiver input that will ultimately inform the development of clinical studies that measure what matters most to patients, such as how patients feel and function in their daily lives.

The topics and questions that each document will address are described below.

Guidance 1: Whom do you get input from, and why? How do you collect the information?

Guidance 1 will discuss several methods to collect patient input. We need to consider the potential research questions and methods when deciding from whom to get input (a sampling strategy). Further in-depth discussion of methods to develop and identify impacts important to patients will be discussed in Guidance 2.

Guidance 2: What do you ask, and why? How do you ask non-leading questions that are well-understood by a wide range of patients and others?

Guidance 2 will provide discussion on methods for gathering information about what aspects of symptoms, impacts of their disease, and other issues are important to patients. It will discuss how to do qualitative research including interviews, interview guides, types of survey questions, and considerations for collecting demographics and survey information. It will also discuss survey methods and qualitative research topics to help avoid misleading results such as inadvertently priming patients in ways that can lead to results that poorly represent what is important to patients.

Guidance 3: How do you decide what to measure in a clinical trial?

Guidance 3 will address refining the list of important impacts and concepts from patients to develop potential study endpoints. Given that not everything identified can demonstrate change in a specific treatment trial or is measurable, how will you select what to measure to show clinical benefit?

Guidance 4: How do you develop or select tools to measure the concepts identified using the methods in Guidance 3? Once you have a measurement tool and a way to collect data using it, what is an appropriate clinical trial endpoint?

Guidance 4 also will address other related questions, including:

1. *How will the tool be administered to patients? You need to decide how you will use the tool selected in a trial (e.g., pen and paper form patients will fill out, using a website, using a study-provided device, going to an office for measurement).*
2. *When and how frequently should you measure? Daily? Every 8 weeks? For an endpoint, if you are using a daily diary, should you average information over a week? A month? Not at all and use the daily measurements?*
3. *What amount of change makes a difference in patients' lives?*

Answers to these questions are driven by one question: What are the important questions that patients want answered?

Endpoint development is not a linear process. It is highly iterative and can be hard to break up into distinct steps. For example, many of the topics in Guidance 1 are important in any research endeavor. The topics covered in Guidance 2 might be used in an exit survey as part of a trial to gain further insights from participants, or people who choose to not participate in a trial to find out what clinical trial changes may enhance participation.

Importantly, these steps can take place in parallel with drug development or, alternatively, they may take place in the precompetitive setting independent of any specific drug development program. Many patient organizations choose to undertake the work of identifying important and measurable health impacts and developing measurement tools in order to facilitate and pave the way for future drug development.

The science of patient input is constantly evolving and gathering robust and meaningful ***patient experience data*** to inform medical product development is a collaborative process. Many professional groups and research teams around the world have developed and are developing templates, checklists, and guidelines for different aspects of gathering and interpreting patient experience data, and many such documents already exist for patient reported outcomes. As these projects and documents mature, we will be updating our approaches.

With this discussion document, FDA seeks input from patient stakeholders, researchers, medical product developers, and others on how best to communicate FDA's current thinking on approaches to collecting patient experience data. Questions for readers to consider:

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. Many potential research methods are available and not all could be included in the discussion document. Is it clear the Agency 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 timepoints 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?

1.1. Introduction to the Legislation and Series of FDA Guidance for Enhancing the Incorporation of the Patient's Voice in Drug Development and Regulatory Decision Making

This series of guidance documents is intended to facilitate the advancement and use of systematic approaches to collect and use robust and meaningful patient and caregiver input that can more consistently inform medical product development and regulatory decision making. This builds on learnings from the disease-specific PFDD meetings[1] that FDA conducted under PDUFA V as an enhancement of the Agency's implementation of a more structured approach to ***benefit-risk assessment***.[2] The benefit-risk framework recognizes that when FDA reviewers conduct a benefit-risk assessment, they consider not only the submitted evidence related to the benefit and risk outcomes and effects reported in clinical studies but also, importantly, the "clinical context" of the disease. This clinical context encompasses two major considerations: 1) an analysis of the disease condition, including the severity of the condition, and 2) the degree of unmet medical need. FDA recognized a need to learn about the clinical context more comprehensively and directly from the perspective of the patients who live with the disease and are exposed to any available therapies and their caregivers.

PFDD meetings gave FDA a deeper appreciation for the expertise that patients and caregivers can bring to the process and the value of incorporating their voice. Furthermore, FDA concluded that patient input can not only inform the clinical context and provide insights to frame the assessment of benefits and risk but also provide a direct source of evidence regarding the benefits and risks, if ***methodologically-sound*** data collection tools could be developed and used within clinical studies of an investigational therapy. If such evidence can be used as a basis for FDA's assessment of benefits and risks, it could also be incorporated in drug labeling to better inform decisions by patients and doctors at the point of care.

Thus, a primary purpose of this series of four methodological PFDD FDA guidance documents is to provide information and direction to external stakeholders regarding what work FDA would expect to be done to bridge from important early-stage meetings to gain patients' narrative perspectives on the clinical context, to development and use of methodologically-sound data collection tools in clinical trials. These guidance documents will also address Agency expectations regarding what sort of analyses might be conducted as part of this work and what sort of documents might be produced, and when appropriate, submitted to FDA for review.

The four guidance documents that will be developed correspond to commitments under section I.J.1 associated with PDUFA VI[3] under the Title I of FDA Reauthorization Act of 2017. The projected timeframes for public workshops and guidance publication reflect FDA's published plan aligning the PDUFA VI commitments with some of the guidance requirements under Section 3002 of the 21st Century Cures Act of 2016.[4] A description of the timelines for development of the four guidances can be found in **Appendix 1**.

[1] https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/ucm347317.htm
[2] https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/ucm326192.htm
[3] https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/ucm347317.htm
[4] https://www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm563618.pdf

In addition to work related to planning for use of ***fit-for-purpose clinical outcome assessments (COAs)***, successful incorporation of patient input in medical product development should include considerations to facilitate patient enrollment and minimize the burden of patient participation in clinical trials and other research studies. Questions to be considered for this planning may include: What aspects of clinical trials conduct (e.g., informed consent, enrollment, frequency of assessments, assessment burden, patient follow-up) can be better tailored to address the needs and concerns of the patients? What steps can be taken to minimize patient burden due to research participation? Patient input to address these important questions should be collected during the pre-clinical stage and can employ methods that will be addressed in Guidances 1 through 4.

In all cases, the level of rigor of the methods applied needs to be appropriate for the questions the study wants to address and the potential impact of incomplete or misleading results.

1.2. Purpose and Scope of Guidance 1: Approaches to collecting comprehensive and representative patient and caregiver input on burden of disease and current therapy

The purpose of this document is to present methods for collecting information on the patient experience that is representative of the intended population to guide the development and evaluation of medical products throughout the medical product lifecycle. In addition, this document presents a synopsis of methods on how to operationalize and standardize data collection, analysis, and dissemination of patient experience data.

Guidance 1 will include a glossary of terms that will be used in one or more of the four guidance documents[5]. Words or phrases found in the draft Glossary appear in bold italics at first mention within the body of text in this document.

In addition to standard terminology, the goal of this guidance is to provide an understanding of:

- Methods to consider at an early stage in drug development to gain a thorough account of patients' experience and perspective on their disease and available therapy
- Example research objectives and questions (this will be further explored in future guidances as well)
- Factors and approaches to ensure the perspectives of a representative cross-section of the disease-indicated population have been included in the information collection
- Standard approaches to consider for collecting, managing, analyzing and reporting the information

Stated another way, for an identified disease area, the information in Guidance 1 should enable the user to develop a plan that will:

- Identify approaches and methods to collect information from patients and caregivers
- Ensure that the input to be collected is sufficiently representative of the range of clinically relevant diversity in the patient population

[5] The draft glossary of terms has been shared as an attachment to this discussion document.

- Identify methods and necessary steps to develop a plan for analysis and reporting of the information that will be collected

Note that the level of rigor needed for generating patient experience data can vary across studies and will depend on the intended use. Guidances 2 and 3 will go into more depth regarding the kinds of research approaches to consider and will detail suggested approaches for summarization/tabulation, presentation and subsequent submission of the collected information for review (e.g., by FDA). Guidances 2 through 4 can then be used to inform relevant stakeholders of subsequent steps necessary for the development and testing of COAs that may be later implemented in clinical studies.

This document is intended to serve as a focus for continued discussion among FDA, patient stakeholders, drug developers, academic community, and the public. It is anticipated that this document will also provide a foundation for FDA and external stakeholders in the development of subsequent relevant guidance(s) on patient-focused medical product development, as it introduces research methods for the science of patient input as well as key definitions.

Although this document presents methods and approaches for collecting patient experience data, it does not address methods for collecting and analyzing COAs or ***patient preference information***. 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*.[6]

1.3. Patient Experience Data

What is patient experience data? Patient experience data is defined in Title III, Section 3002(c) of the 21st Century Cures Act as data intended to provide information about impact (including physical and psychosocial impacts) of a disease or condition, or a related therapy or clinical investigation. Patient experience data can be interpreted as including (but is not limited to) the experiences, perspectives, needs and priorities of patients related to: 1) the symptoms of their condition and its natural history; 2) the impact of the conditions on their functioning and quality of life; 3) their experience with treatments; 4) input on which outcomes are important to them; 5) patient preferences for outcomes and treatments; and 6) the relative importance of any issue as defined by patients.

Others have defined patient experience in similar ways. The patient experience in a medical product development context incorporates the patient's journey throughout the course of their disease or condition including patient views, feelings, needs, actions, preferences, interactions (e.g., clinical trials, home life, social life, etc.) with respect to their disease and its treatment (Wolf et al., 2014; McCarthy et al., 2016).

[6] Guidances are updated periodically. For the most recent version of a guidance, check the FDA Drugs guidance web page: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

The patient's journey should be defined from the patient perspective informed by input from patient partners and clinicians. A patient partner may be an individual patient, caregiver or patient advocacy group that engages other stakeholders to ensure the patients' wants, needs and preferences are represented in activities related to medical product development and evaluation (Wilson et al., 2017). **Figure 1** describes types of patient partners.

Figure 1. 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.

There are different parts of the patient experience to collect and/or measure in medical product development, which may include but are not limited to (Milken Institute, 2015):

- Signs/symptoms of disease or condition
- Chief complaints (most bothersome signs/symptoms)
- Burden of living with a disease or condition
- Burden of managing a disease or condition
- Burden of participating in clinical studies
- Impacts from disease or condition on activities of daily living and functioning
- Impacts from treatment on activities of daily living and functioning
- Views on currently available treatment options
- Views on unmet medical need
- Disease progression, severity, and chronicity
- Natural history of disease or condition
- Minimum expectations of benefits
- Tolerance for harms or risks
- Acceptable tradeoffs of benefits and risks (i.e., patient preference)
- Attitudes towards uncertainty

Information collected on patient experience will be referred hereon as patient experience data**.**

Can data be collected from other experts as well? To supplement patient experience data, FDA recommends also gathering input from clinicians and other experts in the given disease area to ensure endpoints are clinically relevant.

Who can collect and submit patient experience data? As stated in Title III, Section 3002(c) of the 21st Century Cures Act of 2016, patient experience data can be collected by any persons including (but not limited to): patients, family members and caregivers of patients, patient advocacy organizations, disease research foundations, researchers, and drug manufacturers. The person or group collecting the data needs to be clear in submissions to FDA.

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. The collection of patient experience data is important because it provides an opportunity to inform medical product development and enhance regulatory decision making to better address patients' needs.

When do you collect patient experience data? Patient experience data should be collected throughout medical product development, beginning as early as the discovery phase. Early in development, patient experience data can be used to help identify unmet medical needs and important clinical outcomes to be studied, as well as inform clinical trial design. In early and later stages of development or in the precompetitive space, patient experience data can help inform assessment tool development and selection, as well as analyses and communication of benefit-risk. Work in the precompetitive space can be important to be ready for future clinical trials.

When should patient stakeholders be involved in product development? Patients should be meaningfully involved throughout the medical product development process—not only as study subjects but as partners. Engaging patients actively in the development process can potentially improve rates of trial enrollment and retention and increase applicability to patients (Bower et al., 2014).

How do you collect patient experience data? FDA recommends using qualitative, quantitative, or mixed methods (use of both qualitative and quantitative methods in the same study) to collect robust and meaningful patient experience data. These methodological approaches are discussed in **Section 3** of this document and **Appendix 6**. Some key distinctions between each method are shown in **Table 1**. Factors to consider when selecting an appropriate methodological approach are discussed in **Section 2**.

Patient experience data can be collected in a variety of research settings, including (but not limited to): clinical trials; observational studies, including survey studies. The level of rigor needed for patient experience data generation can vary across study and will depend on the intended use. As such, it is important to begin early discussions with FDA to determine which approach should be used.

Table 1. Methodological Distinctions for Collecting Patient Experience Data

	Methodological Approaches		
	Qualitative Methods	**Quantitative Methods**	**Mixed Methods**
Scientific Question	• ***What aspects are important to patients for measurement and reporting of clinical trial results?*** • Uses direct communication (speech or written form) to explore or confirm the meaning or interpretation of a topic from the participant's perspective (e.g., type of patient experience, such as disease symptoms and/or impacts	• ***How do we design a questionnaire measuring aspects of disease?*** • Uses a tool (e.g., survey or questionnaire) that provides numerical information (e.g., survey or questionnaire score) to explore or confirm an outcome	• ***Do we measure severity or frequency?*** • Uses both the qualitative and quantitative data and approaches in an integrated manner in the same study or a set of related studies
Example	• A group of patients are interviewed to describe their experience with the disease or condition	• A group of patients are surveyed and asked to rate the severity of their disease symptoms using closed-ended questions	• A group of patients are given a survey or questionnaire with both open-ended and closed-ended questions

Source: Adapted from Teddlie & Tashakkori (2009)

How can external stakeholders submit patient experience data to FDA? It is important to remember that patient experience data informs development and evaluation of medical products throughout the medical product lifecycle development. While FDA plays a critical role in medical product development, the Agency is just one part of the process. Depending on what type of patient experience data is collected and when it is collected (e.g., stage of development), other stakeholders who also play an important role in the medical product development process (e.g., drug developers, researchers, etc.) may be appropriate end users.

There are various pathways to (a) submitting patient experience data to FDA and (b) engaging with FDA for discussion. Additional FDA guidance on how to submit patient experience data is under development. Depending on the type of patient experience data and the intended purpose of the data with respect to medical product development, different content and formats may be appropriate for submission. At the minimum, a study report from the research study should be submitted to FDA, but additional information including the primary data captured will be needed (see **Section 4** and **Appendix 2)**.

Specific criteria defining what is most informative and useful for FDA submission should be discussed early and often with the appropriate FDA review division(s), as the level and type of criteria might vary based on how the data will be used. However, in all cases the intended purpose of the patient experience data being submitted to the Agency (i.e., how the data are intended for use in supporting medical product development and regulatory decision making) should be made clear in the submission.

Many existing FDA regulations, guidances, and other standards and requirements pertaining to the capture/collection, transmission, processing, storage, archiving, retention, and submission of data from clinical studies conducted to support a regulatory medical product application (e.g., an IND, NDA, or BLA) or medical product labeling language **also apply** to patient experience data generated in such studies. See **Appendix 2** for a partial list of such regulations, guidance(s), standards, and requirements.

How is patient experience data used for regulatory purposes? Patient experience data is used to help inform clinical trial design, trial endpoint selection, and regulatory reviews including benefit-risk assessments. FDA encourages stakeholders considering to collect and submit patient experience data to FDA to have early interactions with FDA during the design phase of such studies and obtain feedback from the relevant FDA review division.

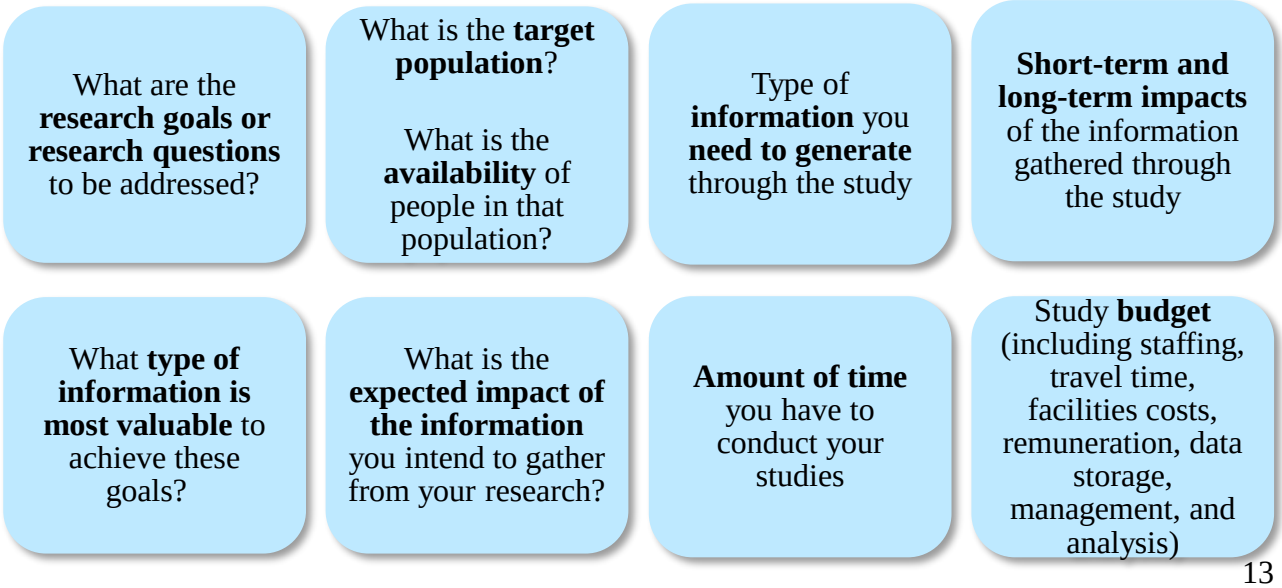
FDA values the use of patient input to help foster the development and availability of safe and effective medical products. The collection of patient input helps FDA gain a better understanding of the patient experience and expected clinical benefit.

2. GENERAL CONSIDERATIONS FOR COLLECTING PATIENT EXPERIENCE DATA

2.1. Overview

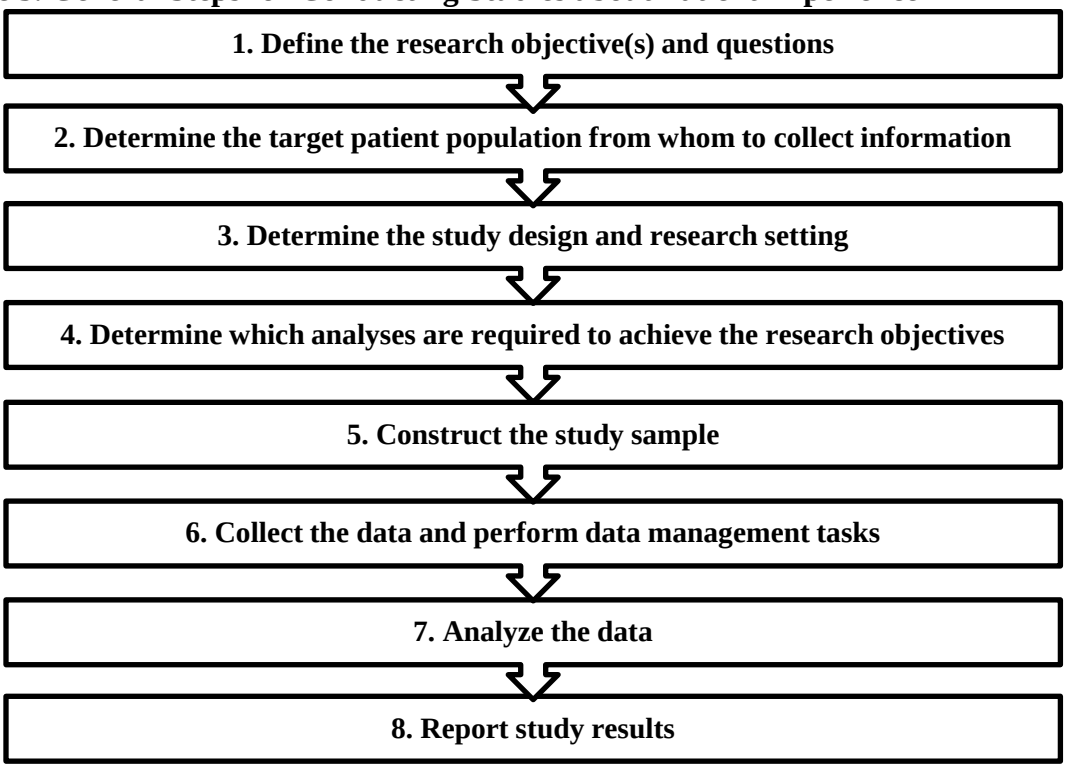
How do you select a research approach? The research approach should be determined during the study design phase, prior to study implementation and should be comprised of the plans for your research as well as the steps to implement those plans. While selecting the appropriate study methods, you should consider the broad research assumptions underlying your study design as well as the detailed elements that should be incorporated into the methodology to meet those assumptions and achieve success (Johnson and Christensen 2017; Teherani, Martimianakis, et al. 2015). **Figure 2** lists the factors that should be considered when selecting a research approach.

Figure 2. Factors to Consider when Selecting a Research Approach



What steps should be used to collect patient experience data? FDA recommends stakeholders follow the general steps listed in **Figure 3**. for studying patience experience. The subsequent sections provide additional details. **The research approach may need to be adjusted based on the answers to these questions.**

Figure 3. General Steps for Conducting Studies about Patient Experience



2.2. Defining the Research Objectives and Questions

How do you define research objectives and questions? Your research objective(s) should be defined by the research questions you are trying to answer. When formulating your research objective, be specific. It may be useful to break down a broader research goal into specific research objectives, aims, and questions. Your research objectives and questions should inform which methodological approaches you use in your research.

When drafting your research questions, you should consult previously conducted studies and other relevant research literature (published and unpublished) along with research and clinical experts. This will help to determine the most appropriate question(s) that will guide your study procedures (Johnson and Christensen 2017). A carefully conducted review on your topic of interest coupled with expert consultation early in the study planning phase will help you clearly identify objectives and questions that will inform:

- which methods are better suited to meet your research goals and provide evidence to support your research questions; and
- the design of study materials (e.g., study protocol, interview guides, coding dictionary).

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.

2.3. Whom to Collect Information from

2.3.1. Defining the Target Population

How do you define the target population? The group of patients whose experience you wish to learn about is the ***target population***. Characteristics of the target population should inform both the type of research methodology and mode of administration that you choose for your study.

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.

More specifics are needed, however. Will the diagnosis be confirmed clinically by the research team? If not what will the source be, self-report, the participants' clinicians, another source? In different situations, different answers may be appropriate. An important factor to keep in mind when choosing a target population is if the research goal is a confirmatory study, or is it more exploratory or hypothesis generating?

2.3.2. Determining Who Will Be Providing Patient Experience Data

Who should provide the patient experience information? FDA generally recommends that the patient directly report their experience with their disease or condition, unless the patient cannot reasonably be expected to reliably self-report (e.g., young children, individuals with cognitive problems, such as Alzheimer's disease, etc.). In such cases, a clinician or other trained health care professional and/or primary caregiver(s), may report on patient experience if it is observable

(e.g., signs of disease or condition, functioning, etc.) (FDA, 2015). Patient representatives and advocates can also provide valuable information about the patient experience.

Who the ***reporter*** is (i.e., the person who will be providing the patient experience information) may vary from patient to patient *within* the target population. You should assess whether multiple reporters are in fact needed within the target population, as well as set criteria to determine when multiple reporters are needed (e.g., determine the minimal age limit at which children can provide reliable responses; determine minimal cognitive function at which individuals can provide reliable responses, etc.). Who the reporter is should be recorded for each report.

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).

Factors to consider if self-report is feasible for patients include (but are not limited to):

- Age
- Level of cognitive development
- Communication skills
- Health literacy
- Insight
- Health state
- Co-morbidities

FDA recommends stakeholders engage with subject matter experts in that disease area when determining the appropriateness of self-report in the target population.

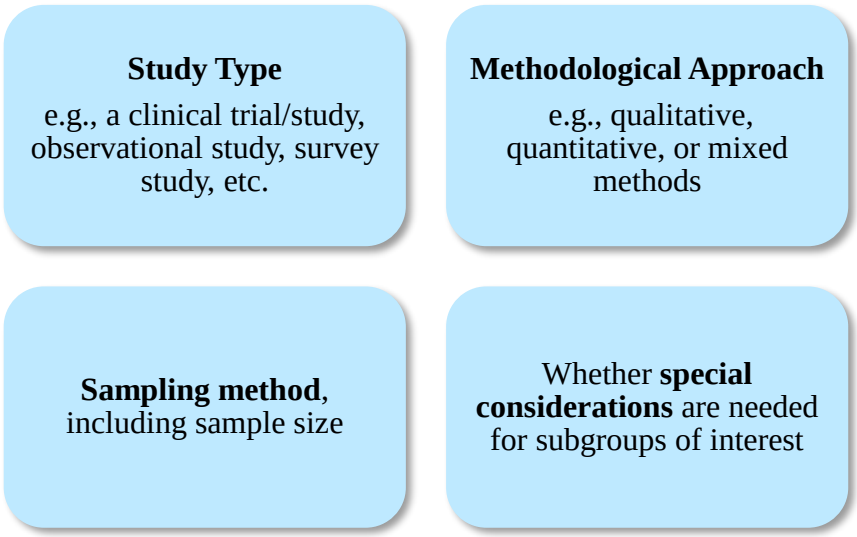
2.3.3. Subgroups

All subgroups of interest should be pre-specified at the study design stage whenever possible. Care should be taken with the number of subgroups being proposed for analysis and inference. Subgroups of interest may be based on reporter type (e.g., patients versus primary caregivers) and/or socioeconomic, demographic, cultural, linguistic, clinical, or other factors pertinent to the disease/condition of interest. For diseases/conditions that manifest with notable symptom heterogeneity, subgroups may be based on the most prevalent (commonly seen) symptoms.

2.4. Determining the Study Design and Research Setting

How do you determine the research study design and setting? Your research study design and setting is determined by your research objectives and questions, which should inform the following.

Figure 4. A Few Study Design Factors



2.4.1. Sampling Methods

There are many sampling methods, each varying in complexity, the use of which depends on the needs and limitations of each situation. FDA recommends stakeholders engage with subject matter experts when determining the appropriateness of sampling methods to use. **Table 2** lists some sampling approaches that may be used to obtain patient experience. They can be classified under two broad types of sampling schemes:

- probability/random sampling and
- non-probability/non-random sampling.

More in-depth discussions of these sampling methods with respect to advantages and disadvantages can be found in the literature (e.g. Johnson, 2015; Groves, Fowler, et al., 2009; Levy & Lemeshow, 2008; Korn and Graubard, 1999; Valliant, Dever, et al., 2013; Fricker, 2008; Heckathorn, 1997; Johnson & Christensen, 2014; and Rothenberg, 1995).

Table 2. Types of Sampling

Type of sampling	Selection Strategy	Examples	Limitations
Probability Sampling			
Simple random sampling (SRS)	A sample drawn by a procedure in which every member of the population has an equal chance of being selected.	A simple random sample is taken from a population of patients admitted to a hospital in the first six months of 2015.	• Can be expensive when units are geographically dispersed and information is obtained through face-to-face interviews. • SRS samples often do not reflect the heterogeneity in the target population.
Stratified random sampling	A sample drawn by dividing the population into mutually exclusive groups and then selecting a random sample from within each group.	Population of prisoners admitted to California prisons are stratified by race and gender and a SRS is taken for each race and gender combination.	• Requires the stratification factors to be known.
Multiplicity sampling	A sample drawn by first taking a probability sample from the target population followed by drawing a sample from the set of individuals who belong to the network of those initially sampled	Current Population Survey Immigration-Emigration Supplement probability samples households each month. Includes question about immediate relatives who had previously lived in the US but are currently living abroad. Enables estimation of emigration rate. (Jensen, 2013)	• The initial probability sampling phase may not be feasible. • Relies on the initial respondents to identify members in their network.
Cluster sampling	A sample drawn by which clusters (i.e., a collective type of unit that includes multiple elements, such as clinical sites in different geographic areas) are randomly selected and either complete- or sub- sampling of individuals within the selected clusters are taken.	A probability sample of hospitals in a state is taken, from which a probability sample of patients from each hospital is taken.	• Often requires information about cluster size as selection probabilities can depend on such information. • Heterogeneity can be compromised if units within cluster tend to be homogeneous.
Multistage probability sampling	Generalization of cluster sampling to include multiple levels/stages of cluster sampling.	CDC Medical Monitoring Project (Frankel et al. 2013). • Stage 1, a probability sample of states. • Stage 2, a probability sample of facilities within each sampled state. • State 3, a probability sample of HIV patients from each sampled facility.	• Often requires information about cluster size as selection probabilities can depend on such information. • Heterogeneity can be compromised if units within cluster tend to be homogeneous.

Type of sampling	Selection Strategy	Examples	Limitations
Non-Probability Sampling			
Snowball sampling (chain-referral)	A sample drawn by which each research participant is asked to identify other potential research participants. The initial sample of individuals is often obtained via non-probability sampling; subsequent samples are obtained by chained referrals from the previous sample.	Patients with sickle cell disease participate in focus groups to discuss symptoms of the disease and impacts of the medications taken. Focus group participants are asked to identify other people they know with sickle cell disease who may be potential research participants so study staff can invite them to join the research study.	• Convenience sample • No basis for generalizability to target population.
Respondent-driven sampling	Similar to snowball sampling. The chain of referrals is often longer than snowball sampling and under certain conditions, estimates can be generalizable to target population (Heckathorn, 2011).	See Heckathorn (1997).	Requires: • A long recruitment chain. • Population is socially networked (Malekinejad et al 2008).
Web-based sampling	A sample drawn by the contact mode (i.e., how the respondents are contacted, such as the web) which can involve multiple sampling strategies (e.g., systematic sampling, multiplicity sampling, list-based, entertainment polls, un-restricted self-selected surveys, volunteer (opt-in) panel).	Researcher selects patients from a web-panelist (e.g., online polling panel) to include in study	• Limited by pre-registered panelists • Selection bias • Potential response bias
Purposive sampling	A sample drawn by which the researcher specifies the characteristics of the population of interest and locates individuals with those characteristics.	Researcher is interested in studying adult females with acne	• Researcher bias (researcher selects the sample)
Convenience sampling	A sample drawn by including people who are available, volunteer, or can be easily recruited in the sample.	Patients who can travel to attend Patient-Focused Drug Development (PFDD) meetings	• Sample can have biases that both over- and under-represent the overall population • Researcher bias
Quota sampling	A sample drawn by which the researcher determines the appropriate sample sizes or quotas for the groups identified as important.	Researcher chooses their sample to consist of 45% females and 55% males to maintain the correct proportions representative of the target population.	• Sample has not been chosen using random selection (impossible to determine possible sampling error) • Unable to make statistical inferences from the sample to the population

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What is representativeness? An important goal is obtaining patient experience data that are not only relevant, objective, accurate, but also representative of the target population. In this document, the term *representative* can be interpreted in the following ways. Depending on the research question you need to consider what impact information, and potential missing information, will have on the usefulness of the gathered patient experience data.

(1) **A sample is representative of the target population if statements made about patient experience based on data from the sample of patients is generalizable to the target population.** Probability sampling schemes enable you to obtain such representative samples and often arise in the context of quantitative studies. However, if groups of patients from the target population are not adequately represented in your study sample, your ability to generalize your research findings to the target population may be limited, even if you use a probability sampling scheme. To some extent, this can be alleviated by oversampling such groups as part of the sampling plan.

(2) **A sample is representative of the target population to the extent that patients in the study sample consists of individuals of various characteristics that to some degree approximate the heterogeneity of characteristics in the target population.** However, statements made about patient experience based on data from the sample are not necessarily generalizable to the target population. Studies in which generalization to the target population is not the primary objective often use non-probability sampling schemes.

The necessary components for probability sampling are shown in **Figure 5**.

Figure 5. Components for Probability Sampling

The listing of individuals is often referred to as the sampling frame. Ideally, the sampling frame should enumerate all individuals in the target population. A random number generator can be used to randomly sample individuals from the sampling frame which in principle produces a sample of patients whose experiences are said to be representative of the target population.

> **Example**: Suppose the target population consists of 100,000 Parkinson's disease (PD) patients alive in the US and each individual is enumerated in a sampling frame with a label of 1 to 100,000. A sample of 2000 patients is randomly selected from among the 100,000 patients and their experiences are ascertained. By virtue of random sampling, statements made about patient experience based on the 2000 individuals in the sample are also valid for the entire 100,000 PD patients.

Non-probability sampling, however, does not require a listing of the entire target population nor does it require a random device to sample individuals. Note also that in some cases, probability sampling can be accomplished without the availability of a formal sampling frame prior to study initiation as it may be constructed as part of the study.

2.4.2. Sample Size

How to determine the sample size for your study? Sample size estimates are driven:

- research objectives
- type of outcomes under consideration
- study design
- planned methods of analysis
- whether the study is quantitative or qualitative in nature.

Having an insufficient sample size may produce unreliable and/or imprecise results. FDA recommends that if the sample size is limited due to practical considerations (e.g., rare diseases), the research objectives should be adjusted accordingly and noted as a limitation in the study report. In practice:

- the number of sampled individuals completing the study can be substantially small,
- there may be interest in one or more subpopulations, and/or
- the study design may be complex.

Sample size calculations should take these features into consideration. If the goal of the study emphasizes both the target population and a subpopulation within the target population, then the sample size should be chosen to satisfy the criteria underlying the sample size calculations for both the target population and the subpopulation inference.

2.4.2.1. Studies Using Quantitative Methods

For quantitative studies, the criteria for sample size calculation are usually quantifiable.

> **Example**: In efficacy superiority clinical trials comparing two or more arms, some of the common statistical specifications for determining sample size are:
>
> - attaining a pre-specified power (e.g., sensitivity to detect a treatment effect of at least 80%, if the effect exists), and
> - minimizing the chance of false positive results (e.g., type I error at most 5%).

For studies focusing on a single population, sample size calculation may be based on precision criterion such as relative error. Sample size calculations for different sampling types, study types, and data types can be found in the literature (e.g., Levy & Lemeshow, 2008; Chow et al., 2008; Thompson, 1987). For complex designs where sample size formulae do not exist, simulation could be used.

2.4.2.2. Studies Using Qualitative Methods

For qualitative studies, sample size determination is often less formal and based on the concept of saturation, which roughly means little new information (i.e., new concepts of importance and relevance to subjects and research question) is gained by recruiting additional patients (Francis et al 2010; Dworkin 2012) and the group of patients thus far recruited appears to be representative. As such, sample size formulae for such studies are often unavailable. Although sample size determination for qualitative studies is usually subjective, there is some guidance in the literature (e.g., Frances et al., 2010; Sandelowiski, 1995; Dworkin, 2012; and references therein).

2.5. Constructing a Sampling Frame

Construct a sampling frame? Without a sampling frame, it is difficult (and potentially infeasible) to sample from the target population. To the extent that disease registries are inclusive and regularly-updated, they can provide a natural sampling frame. Some disease registries may be at the state level, some may be national or international, and some may be local to an organization such as a hospital or a chain of hospitals owned by a particular organization or part of a network. With such registries, care must be taken to exclude people who have died.

For many disease areas, however, registries may not exist or may not be inclusive or well-maintained. In such cases, you may have to devote resources to construct the sampling frame.

> **Example**: In the United States, physician listings such as the AMA Masterfile or state licensing board files has the potential to be used to create a sampling frame for the target population in the sense that a sample of physicians from these sources may be used to elicit members of the target population.

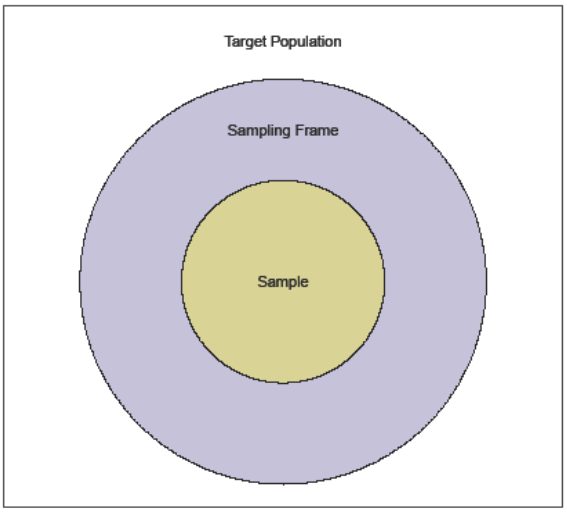
In the above example, unless all physicians treating patients are sampled, and all relevant patients under the care of each physician are identified, the resulting sampling frame may exhibit undercoverage in the sense that not every member of the target population is counted in the frame. **Figure 6** illustrates the concept of undercoverage. The target population of interest is the square. Undercoverage occurs because a proportion of members of the target population is not included in the sampling frame, the large circle. In general, under-coverage may not be problematic if:

- members excluded from the frame could be reasonably viewed as not being substantially different from those enumerated in the frame, and

- the primary goal of the study is to understand the distribution of the patient experience in the target population, rather than to estimate total number of people that hold certain views and preferences.

Regardless, attempts should be made to minimize under-coverage so that the patient population in the frame is not different from the target patient population. In some cases, it may be possible to conduct a screening study to identify members of the target population and create a sampling frame. Additionally, sometimes multiple frames may be used.

Figure 6. Example Undercoverage Sampling Frame



2.6. Additional Considerations to Achieve Sufficient Representation

How do you achieve sufficient representation? Sufficient representation is achieved through careful construction of a sampling frame and choice of an appropriate sampling scheme. However, there are scenarios in which probability sampling may not be feasible. Regardless of how the study sample is constructed, it is important to try and ensure that patients in the study sample represent the target population—to the greatest extent possible with respect to the variables that can affect the outcome of interest. **Figure 7** shows some factors to consider to achieve sufficient representation.

Figure 7. Factors to Consider to Achieve Sufficient Representation

Socioeconomic and demographic background

- Include persons from all relevant demographics within the target population, including: age, sex, race/ethnicity, level of education, socioeconomic status to the extent possible.

Cultural background and spoken language(s)

- Include persons from all relevant cultures and languages within the target population to the extent possible
- Ensure that results from the research study apply to the entire target population. People from different cultures may describe their signs and symptoms of a disease or condition differently and/or may have different values and preferences.

Literacy and health literacy

- Include persons with all levels of reading, writing, problem solving abilities to the extent possible. Also consider person's speaking ability.

Clinical characteristics

- Range of severity of disease or condition
- Range of symptoms and/or functional impacts experienced (especially for those diseases or conditions with symptom heterogeneity, such as migraines and some rare diseases
- Range of physical and cognitive abilities

3. METHODS FOR COLLECTING AND ANALYZING PATIENT EXPERIENCE DATA

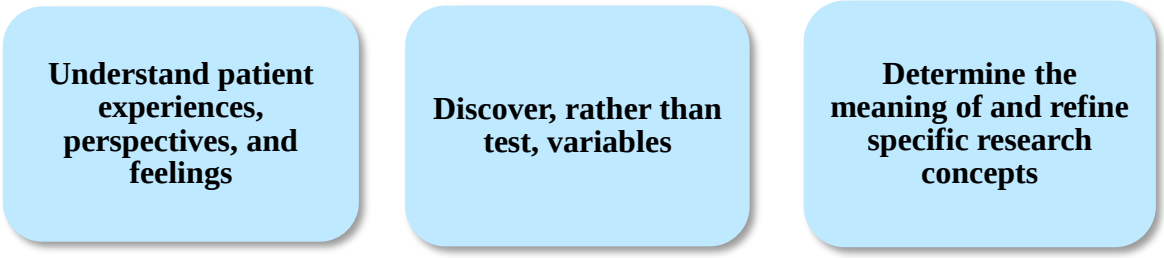
This section provides an overview of various methods for collecting patient experience data. As noted in **Section 1.3**, three main research approaches are commonly used to help guide the collection of patient experience data: qualitative research, quantitative research and mixed methods research (Johnson and Christensen 2017). Additional discussion on these methods can be found in **Appendix 6**.

3.1. Qualitative Research Methods

What are qualitative research methods? The short answer is this is when we talk to people, but to be research, we need structure. Qualitative research methods are generally an exploratory approach used to gain insight into the patient experience and to better understand the meaning of research concepts (Johnson and Christensen 2017; Neuman 2014; MSF 2002). Qualitative methods generally serve to provide answers for the "what," "why," and "how" rather than the "how many" or "how much" in order to generate in-depth information about the experiences, perspectives, and feelings of patients and other individuals (e.g., clinicians, caregivers), in their own words. Qualitative methods are used to elicit information related to research questions, whether it is to better understand burden of disease and/or treatment, or instrument design and feasibility.

Ultimately, qualitative research is a fluid, dynamic and evolving process. **Figure 8** shows the key outcomes from this method.

Figure 8: Key Outcomes from Studies Using Qualitative Methods



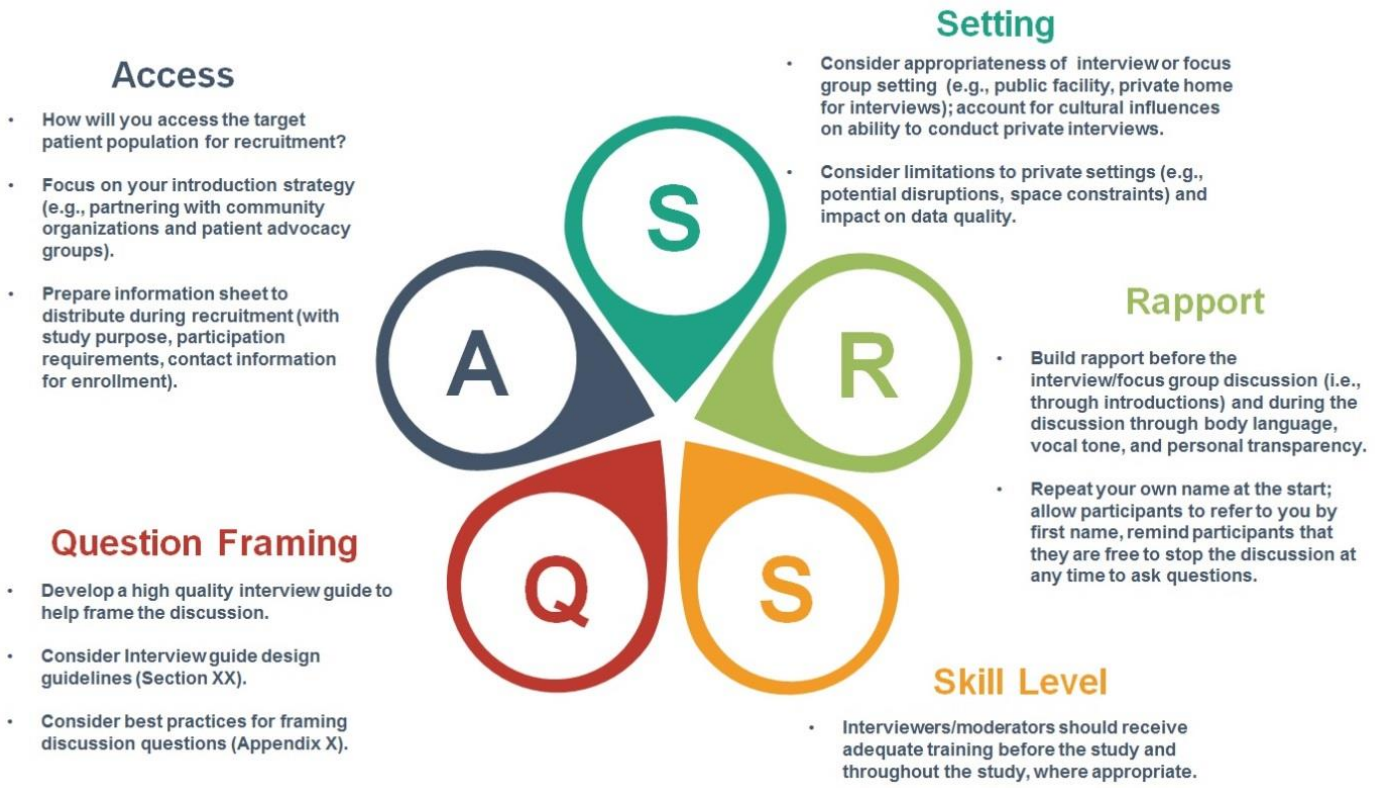
3.1.1. Sources of qualitative data

How do you generate qualitative data? Sources of qualitative data collection include interviews (e.g., one-on-one interviews, focus groups, etc.) and consensus panels (e.g., Delphi panels). FDA recommends that you select the source that meets the needs of your study (including your available resources). **Appendices 3, 4, and 6** describe some common sources, considerations, advantages, and disadvantages of qualitative data (Johnson and Christensen, 2017; Edwards and Holland, 2013; Kvale 1996; McNamara, 1999) and mode of interview administration (e.g., in-person, telephone, video).

3.1.1.1. Considerations for Successful Interviewing and Focus Group Moderation

FDA recommends you use best practices when interviewing and moderating focus groups. While it is difficult to provide a comprehensive list of rules for good interviewing or moderating techniques, below you will find some practical considerations for planning and conducting interviews and moderating focus groups (Johnson and Christensen 2017; MSF 2002). **Figure 9** illustrates factors to consider for successful interviewing and focus group moderation.

Figure 9. Considerations for Successful Interviewing and Focus Group Moderation



3.1.1.2. Social Media

FDA encourages external stakeholders to explore the use of social media tools (e.g., medical community blogs; crowdsourcing; social media pages, such as Twitter, Facebook; etc.) to shed light on patients' perspectives regarding symptoms and impacts of a disease or condition. Targeted social media searches may be useful during the preliminary stages of a study to complement literature review findings, inform the development of research tools (e.g., qualitative study discussion guides) or as a supplement to traditional qualitative research approaches (e.g., one-on-one interviews, focus groups). If social media tools are used to collect patient experience data, they should not be relied upon as a primary source of data. FDA recommends that social media data be used as a complementary supplement to other traditional qualitative data sources (e.g., literature, interviews, or expert opinion).

While social media tools can provide useful data, limitations related to sampling need to be considered. With most social media sources, there is no mechanism for verifying patient identity, or clinical and demographic characteristics; you must rely on patient self-identification and diagnosis, which can be inaccurate. Likewise, different demographic groups tend to use different types of social media (e.g., Pinterest is often dominated by female users, Instagram is dominated by young adults, etc.). Based on this variability, you may need to use different social media tools to gather information from the demographic group(s) you are targeting.

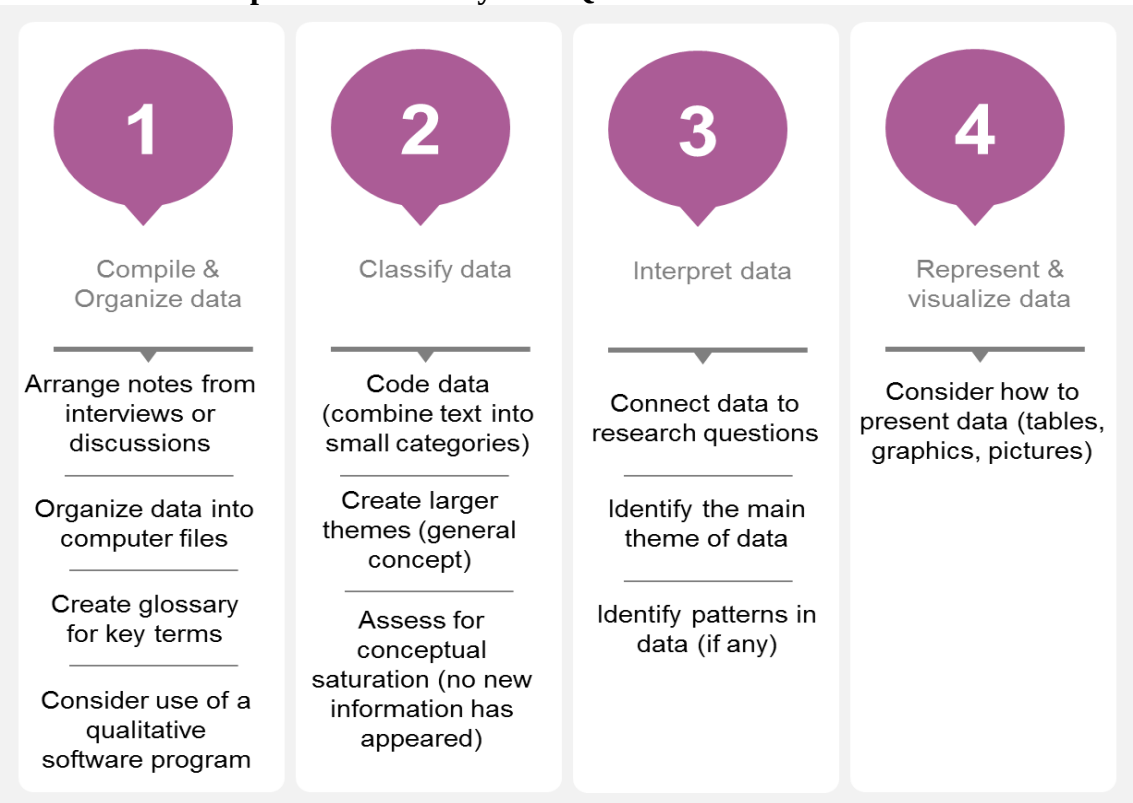
3.1.2. Selecting qualitative methods

How do you determine which qualitative method(s) to use? When selecting your qualitative method, consider how well the individual characteristics of each method match your research goals and the data you expect to generate from your study. Advantages and disadvantages associated with each qualitative data collection method are outlined in **Appendix 6**.

3.1.3. Analyzing qualitative data

How do you analyze data from studies using qualitative methods? FDA recommends stakeholders to consider the general steps outlined in **Figure 10** when analyzing qualitative data. **Appendix 6** expands on these steps.

Figure 10. General Steps for Data Analysis in Qualitative Research



3.2. Quantitative Research Methods

What are quantitative research methods? Quantitative research methods are characterized by the collection of quantifiable data (e.g., numerical data) and the application of statistical methods to summarize the collected data. **Appendix 6** summarizes potential aims of quantitative research.

> **Example:** A group of patients are given a Psoriasis Symptom Questionnaire that includes "closed-ended" questions with a fixed set of response options related to psoriasis symptoms. The Psoriasis Symptom Questionnaire produces a score (i.e. quantitative data).

3.2.1. Analyzing quantitative data

How do you analyze data from studies using quantitative methods? It is beyond the scope of this document to provide an exhaustive list of analytical approaches to analyze quantitative data. Information about missing data, analysis under probability sampling, and software can be found in **Appendix 6**.

In general, however, the analytical approach you take should be appropriate for the:

- research objectives. This is partly related to the aims listed in **Table 9** in **Appendix 6**.
- study design. Potential designs include clinical trials, observational studies, surveys.
- types of data generated in your research study. Some examples include continuous, frequency, categorical, and longitudinal data (**Table 10** in **Appendix 6**).

3.3. Mixed Methods

What is mixed methods? Mixed methods research is where both qualitative and quantitative methods are used. A mixed methods study addresses a set of research questions that require both qualitative and quantitative evidence and methods. Both the quantitative and qualitative data should be analyzed and interpreted together before reaching a conclusion.

Mixed methods studies can occur in different ways: mixing of data, of designs, and of analyses. The simplest approach to a mixed method study involves the mixing of data.

> **Example:** A group of patients are given a survey that is assessing the burden of diabetes. The survey includes open-ended and closed-ended questions. With the use of these types of questions, the survey can produce both qualitative (textual) and quantitative (numeric or categorical) data.

A more complex approach to a mixed method study is mixing of designs. **Figure 11** lists examples of mixed designs.

Figure 11: Mixing Qualitative and Quantitative Components in a Mixed Methods Study

Parallel

- Interviewing participants (qualitative) at the end of a clinical trial or observational survey study (quantitative) to gain insight into the participant's behavior
- Using and analyzing open-ended (qualitative) and closed-ended (quantitative) items as part of the same survey/questionnaire
- Transforming qualitative data into quantitative data through content analysis

Sequential (qualitative first, then quantitative)

- Using qualitative data to define patient subgroups, based on site/field observations of their experience with the disease/condition or treatment (qualitative), and then comparing patients' responses to a survey/questionnaire (quantitative)

Sequential (quantitative first, then qualitative)

- Using additional qualitative data about individuals who demonstrated a clinical benefit versus those who did not in a quantitative analysis to explain their quantitative scores.

Source: Adapted from Yin (2016)

3.3.1. Analyzing data from mixed methods

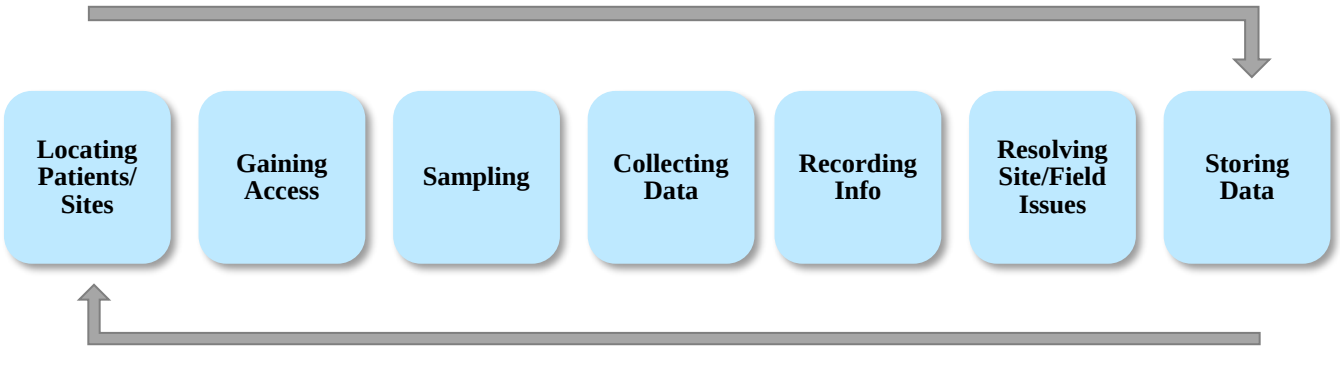
How do you analyze data from mixed methods? Different types of analyses can be used to analyze data from a mixed method study, including combining the use of analyses described for qualitative (**Section 3.1**) and quantitative (**Section 3.2**) methods. FDA recommends that stakeholders choose the best analysis approach for their research objective.

4. OPERATIONALIZING AND STANDARDIZING DATA COLLECTION AND DATA MANAGEMENT

4.1. Standard Approaches to Consider for Collecting and Managing Data

What activities occur during data collection? There are a series of inter-related activities in the process of collecting data (**Figure 12**). FDA encourages stakeholders to carefully plan these activities. Further, FDA recommends stakeholders to standardize data collection activities and data quality issues to the extent possible.

Figure 12. Data Collection Activities



Source: Adapted from Creswell (2013)

4.1.1. Locating Patients/Sites

A critical step in the process of data collection is to identify the appropriate sample and/or sites to study. Patients should not be located at a single site. FDA recommends including patients from diverse sites to provide a complete picture of the topic of interest (see **Sections 2.4.1, 2.5,** and **2.6** on representativeness).

4.1.2. Access

For any study that involves gaining access to sites and patients, external stakeholders should seek permission from a human subjects review board prior to conducting a study and comply with regulations concerning institutional review board (IRB) review and approval, including:

- informed consent requirements;
- Health Insurance Portability and Accountability Act (HIPAA) authorizations
- reporting requirements; and
- maintenance and retention of records.

Studies should be conducted in compliance with Good Clinical Practice, including International Conference on Harmonization Guidelines and consistent with the most recent version of the Common Rule. In addition, these studies should adhere to all applicable local laws and regulatory requirements relevant to the use of medical products.

4.1.3. Sampling Strategy

Of similar importance within the data collection process is the determination of a strategy for the sampling of patients or sites. Refer to **Section 2.4.1** on the different types of sampling.

4.1.4. Collecting Data

FDA recommends stakeholders consider the most appropriate data collection approach for their research objective. Data collection methods can include but are not limited to the following:

- Observations
- Interviews
- Documents (including questionnaires)
- Audiovisual materials

Each of the four data collection methods generates different types of data (see **Table 3**), each of which has its own advantages and limitations.

> **Example:** If data collection for a study only consists of interviewing but the main research objective is to understand how people actually reacted to a given situation (e.g., disease complication, treatment side effects, etc.), the data may be limited to an understanding of the situation as reported by the participants. Depending on the study, these interview data might not provide a full picture of how the people actually reacted, although the data might still show understanding into how participants were thinking about or developed their own understanding of the situation (Yin 2016).

Table 3: Data Collection Methods and Types of Data for Qualitative and Quantitative Research

Data Collection Method	Illustrative types of data	Specific examples of data
Interviews	Language (verbal and body)	A person's explanation of some behavior or action; a recollection; an expressed belief or viewpoint (e.g., email, face-to-face, focus group, online focus group, telephone interviews; Delphi panel)
Observations	People's gestures; social interactions; actions; scenes and the physical environment	The communication between two people; group dynamics; spatial arrangements or a person and a setting
Documents (including questionnaires)	*Contents of*: personal documents, other printed materials, graphics, archival records, and physical artifacts	Public documents (e.g., official memos, minutes, records, archival material); medical records, chart audits; patient/caregiver questionnaires or diaries; photo elicitation (participants take photographs or videotapes)
Audiovisual Materials	Sight and sound (recorded speech or actions)	Videotape or photographs of individuals or groups; sounds (laughter or other vocalized expressions); email or discussion board messages (e.g., medical community blogs); phone text messages or social media pages (e.g., Twitter, Facebook)

Source: Adapted from Creswell (2013) and Yin (2016)

4.1.4.1. Documents (including questionnaires)

Various documents can be used to collect data in obtaining patient and/or caregiver input on burden of disease and treatment (see **Table 3**). Surveys or questionnaires are frequently used particularly in observational studies to capture patient experience data.

What are questionnaires? Questionnaires generally consist of a standard set of questions that are generally administered in the same order to each participant, but can be administered via computerized adaptive testing (Johnson and Christensen 2017). Questionnaires can be administered in both observational studies and clinical trials. In these settings, data can be collected by questionnaires throughout the study or at the end of the study (e.g., exit surveys).

Exit surveys are a standardized method used to collect information about various information, including treatment satisfaction and study experience with minimal recall bias (Geldsetzer, Fink, et al. 2017). Exit surveys are generally administered at the end of a participants' enrollment in a study. However, they also can be administered at any multiple time points throughout the study (Turner, Angeles, et al. 2001; Hrisos, Eccles, et al. 2009).

Questionnaires can be administered in different modes:

- In-person paper administration: paper questionnaires filled out in person by the participant
- Interviewer administration: questionnaire administered by an interviewer following a structured protocol
- Telephone questionnaire administration: questions administered over the phone
- Electronic administration: participants can complete questions via email, web interface, or electronic device

What are some key considerations when using questionnaires to collect patient experience data? Key considerations when using questionnaires to collect patient experience data include the following:

- Each participant in a sample is asked the same set of questions to the extent possible
- Design questions that are interpreted and understood well by participants (e.g., pilot-test questions)
- Avoid using incomplete questions (e.g., Age? Reason last saw doctor?)
- Avoid using questions that ask two or more questions at once (i.e., multi-barreled questions)
- Create distinct and non-overlapping response options for each question

If questionnaires are intended to be used in observational survey studies, FDA encourages the following steps (Cooper, Cooper, et al. 2006):

- Select pool of participants or web-panelists (e.g., health panels) to be observed. Obtain the required permissions needed to gain access to the participants and/or panelists.
- Create a system in which questions can be entered, as well as possible responses, into a database table.

- Generate tables to record the data entered through the questionnaire from the database table of questions and possible responses.
- Develop a simple, user-friendly paper-based or web-based questionnaire.
- Provide data validation during the entry process.
- Develop a coding manual that could be used as a reference document.
- For web-based surveys, generate descriptive statistics that could be observed through the web during the entry phase of the questionnaire.
- Develop program files that allow opportunity to do more advanced statistics once the questionnaire is completed.
- Maintain a database to access the questionnaire table and data entered into the questionnaire. This database should have built-in features or capacity to interface with software that has features such as forms, queries, and reports to further work with the data.

If questionnaires are intended to be a study endpoint in a clinical trial, FDA recommends that stakeholders adopt good measurement principles. Refer to the FDA PRO Guidance on factors to consider when administering questionnaires in clinical trials.

4.1.4.2. Audiovisual materials

Audiovisual materials (e.g., videotape, photographs, social media, etc.) also can be used to collect data in characterizing the patient experience (see **Table 3**).

Steps to consider when using audiovisual materials in the data collection process include:

- Obtain the required permissions needed to use materials.
- Obtain permission to extract information from web content, if necessary (e.g., request permission to join online forums and inquire whether there are restrictions on use of information for research purposes).

4.1.5. Recording information

FDA recommends that stakeholders develop written forms or protocols to collect patient experience data, such as a discussion guide or observational protocol. A discussion guide or observational protocol is a pre-designed form used to record information collected during an interview or observation (e.g., interviewer may take notes on the discussion guide or observational protocol).

4.1.6. Resolving Site/Field Issues

FDA recommends that standardized training is provided to the members of the research team to improve consistency of research. The roles and responsibilities of the team should be outlined in the research protocol. This will help to prevent many site issues. FDA encourages stakeholders to also have a troubleshooting guide. Researcher(s) should anticipate and address site/field issues that might arise during data collection. Examples of these issues are listed in **Table 4**.

Table 4. Site/Field Issues

Access to patients/sites
- Patients' willingness to participate in research
- Patient responsiveness
- Appropriateness of a site
- Building of trust and credibility at the field site
- IRB unfamiliar with certain methodologies

Interviews
- Mechanics of conducting interviews (unexpected participant behaviors, sensitive issues, inexperienced researchers)

Paper Questionnaire Administration
- Quality control at the visit (e.g., researchers or site staff failing to check and gain clarity responses in the presence of the participant)

Web-based Questionnaire Administration
- Consistency in data monitoring procedures and follow-up (e.g., monitoring for timely completion and attrition)

Observations
- Consistency in the role of observer
- Mechanics of observing (remembering to take site notes)
- Recording accurate quotes/notes
- Managing information sufficiently at site
- Funneling information from the observations appropriately

Documents and Audiovisual materials
- Locating materials
- Obtaining permission to use materials
- Minimal noise disturbance
- Best location for video recorder/camera

Ethical issues
- Informed consent procedures
- Dishonest or hidden (secret) activities
- Confidentiality toward participants
- Benefits of research to participants over risks

Source: Adapted from Creswell (2013)

4.1.7. Data Management

FDA recommends that data management is addressed in the early stages of a research study. Before initiating data collection, consider formulating a data management plan (DMP)—a written document that describes the data you expect to acquire or generate during your research study; how you intend to manage, describe, analyze, and store said data; and what mechanisms you will use at the end of your study to preserve and share your data (Stanford University Libraries n.d.(b)). Creating a written DMP helps formalize the data management process, identify potential weaknesses in the DMP, and provides a record of what you intend(ed) to do (Stanford University Libraries n.d.(b)). See **Appendix 5** for resources to consider when developing a data management plan, as well as components of a good data management plan.

4.1.8. Data Standards

FDA recommends that external stakeholders use appropriate data standards to the extent possible when collecting, managing, and reporting patient experience data. See **Appendix 2** for some data standards resources.

4.1.9. Monitoring and Quality Assurance

FDA expects that external stakeholders will be responsible for monitoring the study, ensuring data integrity, and performing the data analysis.

4.1.10. Storing Data

FDA recommends that external stakeholders plan how to store their data in advance of starting their study. Researchers should decide how data will be best stored so that it can be easily retrieved and protected from any type of damage or loss. The approach to data storage should reflect the type of data collected. In regards to the length of time to keep records of data, researchers should comply with their IRB and appropriate regulations.

Principles to consider about data storage and handling data include the following (Creswell 2013):

- Create back-up copies of computer files
- Use high-quality equipment for audio-recording information during interviews
- Protect the anonymity of participants by de-identification
- Create a data collection table or database to track and identify data
- Maintain a list of types of data collected

4.1.11. Confidentiality

All personal participant data collected and processed for research should be managed by the research team with adequate precautions to ensure confidentiality of the data in accordance with applicable national and/or local laws and regulations on personal data protection.

5. CONCLUSIONS

This document has provided an overview of methods to collect robust, meaningful, sufficiently representative patient input to inform medical product development and regulatory decision making. The proposed methods presented serve only as a basis for dialogue in the evolving and growing area of the science of patient input.

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