Patient-Focused Drug Development: Methods to Identify What Is Important to Patients

Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

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This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

A. Overview of the Series of FDA Guidance Documents on Patient-Focused Drug Development

This guidance (Guidance 2) is the second in a series of four methodological patient-focused drug development (PFDD) guidance documents[1] that describe how stakeholders (patients, researchers, medical product developers, and others) can collect and submit patient experience data[2] and other relevant information from patients and caregivers to be used for medical product[3] development and regulatory decision-making. The topics that each guidance document addresses are described below.

- Methods to collect patient experience data that are accurate and representative of the intended patient population (Guidance 1)[4]
- Approaches to identifying what is most important to patients with respect to their experience as it relates to burden of disease/condition and burden of treatment (Guidance 2)
- Approaches to selecting, modifying, developing, and validating clinical outcome assessments to measure outcomes of importance to patients in clinical trials (Guidance 3)

[1] The four guidance documents correspond to commitments under section I.J.1 associated with the sixth authorization of the Prescription Drug User Fee Act (PDUFA VI) under Title I of the FDA Reauthorization Act of 2017, as well as requirements under section 3002 of the 21st Century Cures Act (available at https://www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm563618.pdf).

[2] 21st Century Cures Act: https://www.congress.gov/bill/114th-congress/house-bill/34v.

[3] A drug or biological product.

[4] See the guidance for industry, FDA staff, and other stakeholders *Patient-Focused Drug Development: Collecting Comprehensive and Representative Input* (June 2020). We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

- Methods, standards, and technologies for collecting and analyzing clinical outcome assessment (COA) data for regulatory decision-making (Guidance 4), including selecting the COA-based endpoint and determining clinically meaningful change in that endpoint

Please refer to **Guidance 1** and other FDA guidances[5] for additional information on patient experience data.

In conducting research that involves accessing patient experience data or directly engaging with patients, it is important to carefully consider Federal, State, and local laws and institutional polices for protecting human subjects and reporting adverse events. For additional information about human subjects protection, refer to **section IV.A.2 of Guidance 1**.

FDA encourages stakeholders to interact early with FDA and obtain feedback from the relevant FDA review division when considering collection of patient experience data related to the burden of disease and treatment. [6] FDA recommends that stakeholders engage with patients and other appropriate subject matter experts (e.g., qualitative researchers, clinical and disease experts, survey methodologists, statisticians, psychometricians, patient preference researchers) when designing and implementing studies to evaluate the burden of disease and treatment, and perspectives on treatment benefits andrisks.

B. Purpose and Scope of Guidance 2

This guidance will discuss methods for eliciting information from individuals identified in Guidance 1. It will discuss best practices in conducting qualitative research and reference-related resources[7]; however, it should not be viewed as providing detailed instructions on how to use particular methods or as a substitute for engaging subject matter experts when undertaking the work described.

The methods described in this document can be used to elicit what is important to patients, which may in turn help inform understanding of disease/condition and clinical trial design. It may also help the generation and use of patient experience data, including clinical outcome assessments and patient preference information, to inform benefit-risk assessment.

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[5] See FDA guidance for industry *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* (August 2016), or subsequent guidances in the PFDD series, when available.

[6] In addition to the general considerations discussed in this guidance, a study may need to meet specific statutory and regulatory standards governing the collection, processing, retention, and submission of data to the FDA to support regulatory decisions regarding a marketed or proposed medical products. This guidance focuses on more general considerations that apply to many types of studies, and you should consult with the review division and applicable guidance regarding any other applicable requirements.

[7] The citation of a scientific reference in this guidance does not constitute FDA's endorsement of approaches or methods presented in that reference for any particular study. Study designs are evaluated on a case by case basis under applicable legal standards.

This guidance does not address methods for collecting and analyzing COA data, a topic to be covered in later guidance in this series. It also does not address methods for collecting and analyzing patient preference information, which is addressed in other FDA guidances.[8]

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance means that something is suggested or recommended, but not required.

II. METHODS TO IDENTIFY AND UNDERSTAND WHAT IS IMPORTANT TO PATIENTS

A. Background Research

Research to understand what matters most to patients living with a disease or condition to guide medical product development should begin with a characterization of the disease or condition and currently available therapies. Before conducting studies in patients, which may involve their caregivers as well, literature reviews, consultation with relevant subject matter experts, and other information sources should be used to develop targeted research questions and select appropriate methods to identify what matters most to patients regarding their experience with their disease or condition.

B. Overview of Methods

When planning research, consider whether the study sample reflects the group of individuals (patients) of interest (i.e., the target population), including the spectrum of disease or condition and patient diversity, and whether the methods used to elicit information from patients are appropriate for the research objective and target population.[9]

Qualitative research methods, quantitative research methods, or mixed-methods research can be used to identify what is important to patients. These methods can be used either independently or complementarily. When selecting an appropriate research method or set of methods, FDA recommends carefully considering the research objectives:

- Qualitative research methods, such as interviews and focus groups, are typically used to obtain a deeper understanding of the patient experience by generating in-depth

[8] Issues related to patient-reported outcome measures and patient preference information are addressed in the following guidances for industry: (1) *Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims* (December 2009) and (2) *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* (August 2016).

[9] For more information on defining research questions and the target population, see the guidance for industry, FDA staff, and other stakeholders *Patient-Focused Drug Development: Collecting Comprehensive and Representative Input* (June 2020).

information about the experiences, perspectives, priorities, preferences, and feelings of patients and others, in their own words.

- Quantitative research methods, such as surveys, are characterized by the collection of quantifiable data (e.g., numerical data) and the application of statistical methods to summarize the collected patient experience data, to describe, compare, or relate measures of patient experience.
- Mixed methods research, such as a survey instrument with open-ended and fixed-response questions or interviews combined with administration of a survey instrument with fixed-response questions, involves using both qualitative and quantitative approaches or methods in a single study or program of inquiry to understand the patient experience.

Although this document includes distinct sections for qualitative and quantitative research methods, many data collection methods may be used in either approach. For example, interviews are commonly used to generate qualitative data, but they also may be used to generate quantitative data. Similarly, survey instruments are commonly used to generate quantitative data but may also be used to generate qualitative data with open-ended questions.

III. QUALITATIVE RESEARCH METHODS

A. Common Qualitative Methods Used To Obtain Patient Input

One-on-one interviews and focus groups are two common qualitative methods, which will be discussed in this section. Other commonly used qualitative methods are summarized in Appendix 1.[10] There is no single preferred qualitative method for all uses and research questions. The method selected should be suitable for the research objective(s) and question(s). FDA will review the rationale and appropriateness of the qualitative method chosen. Before selecting qualitative data collection methods, consider patient characteristics and potential strengths and limitations of the methods discussed in Table_4 in Appendix 2. There also is not a universal number of interviews and focus groups to conduct; it is dependent on the research objective. For certain methods, it may be guided by the achievement of saturation[11] (see Appendix 4).

1. One-on-One Interviews

One-on-one interviews (i.e., one person interviewing another person) involve a discussion on the topic of interest between the study participant and a trained interviewer. One-on-one interviews offer opportunities to explore topics in-depth at an individual level using probing questions. There are three different types of interview methods: structured interviews (interviewer asks a set of predefined questions), semi-structured interviews (interviewer asks a set of predefined questions and probing questions), unstructured interviews (interviewer asks unplanned or spontaneous questions).

[10] Many of these methods can be accomplished in person or using technology (e.g., social media, online forums, and other web-based methods).

[11] Also referred to as concept saturation, data saturation, or thematic saturation. For further discussion of saturation, see e.g., Bernard and Ryan, 2010; Suter, 2012; Creswell, 2013.

When using one-on-one interviews, it is important to consider the following:

- Patient selection and sample size
  - Selecting sources for participant recruitment (e.g., medical practices/centers, academic institutions, research consortia, polling organizations, national panels), where applicable, to recruit participants for in-person interviews.
  - Choosing an appropriate sampling method (refer to Guidance 1).
  - Estimating an adequate number of interviews to conduct[12], while considering number of sites, as well as geographic and patient representation
    - A greater number may be needed for unstructured interviews, broad or complex topics, or diverse populations.
- Interview and data collection methods
  - Selecting the appropriate interview type and administration method (i.e., in-person or remote) for the target population; see section III.A.3 for more information on administration methods.
  - Designing suitable interview questions and interview guide (focus on concepts of importance for context of use and research objectives).
  - Pilot testing interview guide (i.e., administer the interview in a small number of participants) to identify and correct any methodological or logistical issues before using in the qualitative study.
- Interview conduct
  - Pilot testing length of interview and appropriateness of length for administration method.
  - Selecting and training interviewers to perform interviews (e.g., considering expertise in performing interviews and other factors based on the characteristics of the disease or condition and target population under study).
    - The emotional burden for the respondent (potential for heightened emotions, including anxieties and discomfort among patients and caregivers), as well as the emotional burden for the interviewer (potential for emotional distress associated with hearing about difficult patient and caregiver experiences), may affect responses.

2. Focus Groups

Focus groups involve a conversation with a group of participants led by a moderator. The moderator can explore issues at the individual level, as well as encourage discussions among participants at the group level. This approach elicits a range of experiences.

There are different types of focus groups[13]; however, the most common type is the single focus group, an interactive discussion of a topic by a set of participants and a moderator(s) as one group in one place. Generally, a moderator uses a semi-structured discussion guide to direct the group conversation.

[12] Note the sample size estimated before the study may not match the final sample size.

[13] For additional discussion of focus groups, see Guest et al., 2013; Greenbaum, 2000.

The considerations for focus groups are similar to one-on-one interviews (e.g., choosing an appropriate administration method and sampling method, designing suitable questions and discussion guide, pilot testing the discussion guide and length of meeting). Other important considerations for focus groups include:

- Selecting a trained moderator with the appropriate skills
- Choosing the number of focus groups to conduct, which may vary based on factors such as:
  - Complexity of the topic(s) (e.g., all versus some impacts of a disease or condition on multiple dimensions of a patient's quality of life, dependent upon therapeutic area and research question(s))
  - Sensitivity of the topic(s) (e.g., separation of genders for sensitive topics such as sexual function)
  - Diversity of the participant sample
  - Number of subgroups planned (e.g., different age groups, disease or condition severity groups, gender)
- Determining the sample size for each focus group: generally, the goal is to keep the group small enough to enable the elicitation of in-depth responses from each participant but large enough to get a wide variety of perspectives across different severity levels and demographic representation within the target disease or condition
  - Although there is no set number recommended for a focus group sample, sample sizes between 5 and 10 participants are common.[14]
  - A group may become fragmented (e.g., multiple, simultaneous conversations occur) when there are too many participants, decreasing the likelihood of engagement and responses from each individual.

3. Choosing Between One-on-One Interviews and Focus Groups, In-Person or Remote

Both one-on-one interviews and focus groups may be useful to capture patient experience data. For example, focus groups could be used in preliminary research to explore a broad topic followed by one-on-one interviews to obtain more detailed information on the topic of interest.

Each interview method has its own strengths and limitations. One-on-one interviews can be used to obtain more detailed (in-depth) individual experiences; address sensitive topics; and explore diseases or conditions with many different symptoms that vary from patient to patient (i.e., heterogenous disease/condition presentation). Focus groups allow for participant interaction and can capture a range of perspectives within a population in a shorter time frame.

One-on-one interviews and focus groups can be conducted in-person or remotely (e.g., use of computers or telephones).

FDA does not have a single recommended administration method for conducting interviews and focus groups; however, the method should be appropriate for the selected target population, study characteristics, and study objective(s). FDA will review the rationale and appropriateness of the administration method chosen for the intended use.

[14] For additional discussion on size of focus groups, see Hennink and Levy, 2014.

Each administration method has strengths and potential limitations. A growing body of literature suggests that there are no marked differences between interview administration methods regarding the accuracy of the data collected.[15]

Table 1 lists some potential strengths and limitations for in-person and remote administration methods. Some strengths and limitations are not entirely distinct for the methods.

Table 1. Potential Strengths and Limitations of Administration Methods

Administration Method	Strengths	Limitations
In-person	• Allows for collection of both verbal and nonverbal responses to help inform data interpretation. • A variety of written and brainstorming exercises (e.g., ranking exercises for concept of interest) can be incorporated into the interview/discussion guide to help elicit information.	• Cost can be prohibitive (e.g., travel costs, facility/room space rental fees). • It may be a hardship for patients and/or caregivers to attend in-person (e.g., health status, logistical or economic constraints).
Telephone (audio only)	• Participation is not limited to a geographic location — study sampling can be nationwide or worldwide (i.e., ability to obtain geographically and socially diverse populations). • Participants can be involved in the comfort of their homes or location of their choice. • Useful for participants who are unable to travel, have poor health status, and/or have limited mobility or disability. • No travel costs or facility/room space rental fees.	• A rapport may be difficult to establish between the interviewer/moderator and participant. • Participants may not have a private space to feel comfortable participating. • Disruptions (e.g., background noise and presence of family members) can interfere with sound quality and cause distractions.
Online/virtual video conferences	• Potential for participants to see each other if using a web cam. • Allows opportunity to see facial expressions. • Also, see strengths for in-person and telephone administration.	• Participants need to have access to the appropriate technology (e.g., a computer, webcam, internet service). • Technical problems (e.g., wireless internet signal problems, audio/video issues). • Potential security problems with personal data collection via online. • Potential costs for virtual conferencing platform(s).

[15] Block and Erskine, 2012; Cachia and Millward, 2011; Shapka et al., 2016; Vogl, 2013.

Administration Method	Strengths	Limitations
		• See also the limitations for telephone administration.

B. Approaches To Asking the Right Question

Regardless of method, the way questions are framed is critical to collecting unbiased patient input. Although spontaneous responses are ideal, there are situations in which participants may need to be prompted.

Prompts (i.e., open-ended questions to stimulate and provoke participation in the discussion) are used to help the interviewer/moderator gain more information, particularly if the participant does not initially provide detailed responses. Prompt questions should avoid leading the participant. Leading questions (i.e., questions that include or imply the desired answer to the question in the phrasing of the question) are problematic because they may result in biased or false/misleading answers (results). They may also lead to a missed opportunity to hear an unexpected insight.

Approaches to *avoid* leading questions include (but are not limited to):

- Do not suggest an answer.
- Do not assume you know what the participant is thinking or feeling.
- Do not ask questions that cast judgment on a participant's belief, choice, or perspective, or imply that you prefer the participant to respond in one way versus another.

The boxed text that follows offers some examples of probing questions or prompts that are leading or otherwise problematic and offers potential solutions.

EXAMPLES

Example 1
Research Objective:

Determine what aspects of peripheral artery disease patients would like to see improved with treatment.

Leading Probing Question:
Wouldn't you consider it most important to improve your walking distance, for example, how far you walk around the track when you exercise?

Problem: This question guides the respondent to provide an answer that is more favorable or preferred by the researcher. Additionally, the *for example* clause may not include relevant examples for the research participant.

Potential Solution: Consider rephrasing as:
Tell me how peripheral artery disease impacts you. What would you like to see improve with treatment?

EXAMPLES
Example 2 **Research Objective:** *Determine what factors to consider when deciding whether to treat your condition with medication.* **Probing Question That May Be Perceived as Casting Judgment:** *"Could you tell me why you are not treating your condition with medication?"* **Problem:** This question implies that the interviewer is potentially casting judgment on the participant's beliefs or choices. **Potential Solution:** Consider rephrasing as: *What did you consider when deciding whether to treat your condition with medication?*

IV. QUANTITATIVE RESEARCH METHODS

Survey research methods are commonly used to collect quantitative data from patients and relevant stakeholders. Refer to **Guidance 1** for considerations for data management and data analysis (including data analysis plans). In designing a survey instrument, it is important to decide how to administer the survey instrument and how to design and test the instructions, questions, and response options.

A. Choice of Survey Administration Method

Survey instruments can be self-administered or interviewer-administered. Self-administered surveys can be paper-based, telephone-based (e.g., interactive voice response system), or electronic-based (e.g., computers, tablets, smartphone). Interviewer-administered surveys can be conducted in-person or remotely.

Choice of administration method may be driven by a variety of factors. For example, an interviewer-administered survey instrument, a survey instrument using an interactive voice response system, or a survey instrument easily completed using common assistive technology on a computer may be useful in patients with visual impairment.

Self-administration allows participants to respond at their own pace and at their convenience. Compared to interviewer-administered surveys, self-administration typically is less costly and removes the potential for interviewer bias. Computer-assisted and administered survey instruments can navigate skip patterns, help minimize missing data, and allow real-time data collection and analysis compared with other methods.

Administering survey instruments in a clinical trial at screening and/or exit visits (e.g., occurs at or after the end-of-treatment visit or last clinic visit) may add greater depth to understanding the burden of disease or condition, treatment, and trial participation, as well as provide more detail on patients' perspectives on treatment benefits and harms, which may help inform drug development (e.g., future clinical trial design) and COA development (see Appendix 5).[16]

[16] For a discussion of additional steps to consider when administering survey instruments in noninterventional studies, see Cooper et al., 2006.

B. Considerations for Developing Questions and Response Options for a Survey Instrument

Survey instrument instructions and questions should be: [17]

- Well-aligned with the research objective(s) and designed to answer the research questions
- Specific to the targeted concept for the research question (e.g., disease/condition symptoms and impacts, current treatment, past treatments, treatment side effects) with minimal redundancies across questions
- Well-understood by participants to enhance consistency of response, including having been:
  - Assessed for appropriateness for the ability of the population (e.g., reading and writing ability (literacy); ability to understand health information (health literacy); and ability to understand and use numbers (numeracy)_)
  - Developed to include natural, familiar language (e.g., minimal use of clinical terminology) as used by patients when discussing the concept of interest
  - Assessed for translatability of questions if used in multinational and multicultural studies; ultimately, the survey instrument should be translated and culturally adapted for all languages and cultures where it will be administered[18]
  - Assessed for applicability of the content (although sometimes a *not applicable* response option is also needed for a question)
  - Tested through interviews of respondents in the target population to make sure they interpret the survey instrument instructions, questions, and responses as intended and can respond accordingly (including that question stems and response options are appropriate and meaningful); alternatively, tested through the survey instrument (e.g., inclusion of survey questions to measure comprehension of attributes, questions, and concepts in a format that can be analyzed so that comprehension is part of the main analysis)
- Formatted in a simple manner to maximize the ease of use for respondents and interviewers
- Assessed for potential response bias (e.g., the tendency of respondents to answer questions in a manner they perceive may be viewed favorably by others)
- Tested to ensure electronic or web-based technology is functional and/or compatible to administer the survey instrument, if applicable
- Scripted to ensure standardization, if administered by an interviewer

FDA discourages the use of:

- Incomplete questions (e.g., Age? Reason last saw doctor?)
- Leading questions

[17] Questions for survey instruments can be generated from multiple sources, e.g., standard textbooks (e.g., Streiner et al., 2015).

[18] Additional considerations regarding translation and culturable adaptation of survey instruments can be found in Survey Research Center, 2016; Wild et al., 2005.

- Unclear or confusing questions (i.e., poorly worded questions)
- Double-barreled or multi-barreled questions (i.e., a question that asks about two or more concepts at once)
- Double negatives (i.e., a sentence that includes two negatives)

When developing questions, consider the respondent effort to complete the survey instrument because this effort can contribute to respondent burden, which can result in lower-quality data and nonresponse. Minimize respondent burden by including a simple survey design and layout (including simple questions), nonrepetitive questions, pretesting of questions, and time testing (estimate time to complete survey).

EXAMPLES

Double-Barreled Question:

How embarrassed and self-conscious have you been because of your condition?

The question above is asking about two different concepts in a single question (i.e., presents two questions in a single question).

Combining these concepts into one question makes it unclear what is being measured. Once respondents answer the question, it likely will be impossible to know which concept the respondents were thinking about when they answered the question (unless it was an interviewer-administered question and further probing was done).

One way to address this issue is to split the question into two or more parts. For example,

1. How embarrassed have you been because of your condition?
2. How self-conscious have you been because of your condition?

Double-Negative Question:

Do you agree or disagree with the following statement? "I do not have symptoms that are not of concern."

The question above uses two negatives in one question, which may cause misinterpretation from respondents.

One approach to address this issue is to avoid using any negative statements to the extent possible. For example:

Do you agree or disagree with the following statement? "I have symptoms that are of concern."

If the double negative is unavoidable, the question should be pretested to ensure that respondents have a clear understanding of the question. In some cases, the negative word may need to be underlined to catch the participant's attention.

It is also important to note that negative questions (single- and double-negative questions) are difficult to use with administration methods where there is no visually accessible (i.e., visible) question (e.g., telephone or interactive voice response systems). Negative questions may also lead to challenges when translating questions. Instruments should be developed so that they have the potential to be implemented across all methods of data collection.

There are two types of questions that can be used in survey instruments:[19]

- Closed-ended questions (questions with fixed set of response options)
- Open-ended questions (questions without a fixed set of response options, e.g., free text)

Table 2 lists examples of closed- and open-ended questions, as well as some strengths and potential limitations of using different question types.

Table 2. Some Potential Strengths and Limitations of Open- and Closed-Ended Questions

Question Type	Examples	Strengths	Limitations
Closed-ended questions	Which of the following health conditions do you currently have? • Asthma • Acne • High blood pressure • Glaucoma	• Respondent typically can reliably answer the question when response options are given • Researcher typically can reliably interpret answers • May be easy and quick for respondents to record answers	• May not provide respondent with a comprehensive list of response options • Response options may not be applicable to the respondent
Open-ended questions	What health conditions do you have?	• May obtain answers that were unplanned • Provides opportunity for respondents to answer questions in their own words	• May be challenging to analyze

Table 3 examines some different types of response options; note that this is not an exhaustive list.

Table 3. Response Options

Response Option	Examples	Limitations
Checklist	Please check to indicate if you ever had any of the following conditions (please select all that apply): ☐ Diabetes ☐ Kidney disease ☐ Stroke ☐ High blood pressure ☐ Asthma ☐ Heart attack	• Checklists may not cover all the possible responses or may not be applicable to all respondents. Adding an "Other" response option with an associated free text box at the end of the checklist may minimize this limitation.

[19] These types of questions also can be asked in interviews and focus group discussions.

Response Option	Examples	Limitations
Dichotomous (two-response options)	Have you ever been diagnosed with glaucoma? • Yes • No I have been diagnosed with glaucoma. • True • False	• May force respondents to choose between a narrow set of response options, resulting in a response that does not completely capture their experiences/feelings
Rankings	Rank the importance of the following characteristics of a treatment for lung cancer (fill in your rank order in the spaces provided using the numbers 1 through 5, with 1 indicating most important and 5 indicating least important). __ Treatment relieves symptoms __ Treatment has few side effects __ Treatment will increase survival __ Treatment can be taken as a pill __ Treatment can be taken monthly	• Ranking scales can be a difficult task for respondents, particularly if there are several response options (e.g., >5) and/or if respondents have poor numeracy skills • Ranking scales do not capture why something is important or unimportant to respondents • Ranking scales address questions in relation to each other rather than individually, which can be difficult for respondents • It may not be possible to measure how much distance there is between levels of importance for each rating.

Response Option	Examples	Limitations
Rating scales	<u>Numeric</u> Rate your pain at its worst in the last 24 hours. • 0 (no pain) • 1 • 2 • 3 • 4 • 5 • 6 • 7 • 8 • 9 • 10 (worst imaginable pain) <u>Verbal</u> Rate your pain at its worst in the last 24 hours. • None • Mild • Moderate • Severe How often have you had pain during the past week? • Not at all • A little • Quite a bit • All the time	• Decreased ability to accurately use rating scales at extremes of age. • Although distances between response categories appear equidistant, the observed distances or change may vary. For example: o The difference between rating pain "2" versus "3" may not be the same difference in pain when comparing "8" versus "9" ratings on a numeric rating scale o The difference between rating pain "mild" versus "moderate" may not be the same difference in pain when comparing "moderate" versus "severe" ratings on a verbal rating scale
Visual analog scale (VAS)	How severe has your abdominal pain been today? (place a mark (I) on the line below) 	• Respondents may be unable to estimate distances on the VAS line precisely • Cannot be administered verbally • Higher rates of missing data (Dworkin et al., 2005; Hawker et al., 2011) • Inconsistencies with the length of the VAS line • Marks may not be clear

The ordering of questions in a survey instrument also may be important. Priming occurs when information presented in an earlier question causes respondents to adjust their responses to subsequent questions.

Ways to avoid priming include the ordering and spacing of questions. The order of questions generally should flow from general to more specific to avoid order bias.[20] Appropriate spacing

[20] For additional details on order bias, refer to Browne and Keeley, 1998.

of questions (e.g., separate topics on different pages or electronic screens) can also minimize response bias.

The use of screening questions can result in priming; however, in some instances, a screening question may be useful to ensure that the survey instrument is appropriate and relevant to the respondent.

EXAMPLE

Scenario: A survey instrument has been designed to assess the burden of using a colostomy bag (stoma bag).

A screening question would be useful to avoid including survey respondents in which this subject matter may not be of relevance.

Screening question: *Do you currently use a stoma bag? Yes/No*

V. MIXED METHODS

Studies using mixed methods research can use a sequential or concurrent design to explore or confirm a concept of interest.[21]

EXAMPLES

Example 1
Mixed methods study based on a qualitatively driven sequential design
A qualitative study uses focus groups to gain broad insight into patients living with diabetes. Following the focus groups, one-on-one interviews are conducted in a different set of individuals to obtain a deeper level of understanding of the experiences and feelings of patients with diabetes. The information from this qualitative research (i.e., focus groups and one-on-one interviews) is subsequently used to develop a diabetes-specific survey instrument to better understand the prevalence of the generated concepts in a larger patient population.

Example 2
Mixed methods study based on a quantitatively driven sequential design
A study explores depression and anxiety in patients with acute coronary syndrome (ACS) by administering a survey instrument to patients with ACS (quantitative component). Analyzing the survey data, researchers find an association between depression and anxiety for female patients with ACS. In the second phase of the study, the researchers conduct follow-up qualitative interviews with a sample of the patients, targeting depressed male and female patients with ACS, to explore why the relationship appeared to be present only for female patients (qualitative component).

Example 3
Mixed methods study based on a concurrent design
A study examines the patient experience with living with amyotrophic lateral sclerosis through one-on-one interviews with patients and caregivers (qualitative component). Within the study, there is concurrent collection of symptom checklist data (quantitative component). The data from both study components are analyzed separately before being compared.

[21] For additional details on how to design and operationalize mixed method measurement studies, refer to Johnson and Christensen, 2014; Johnson and Christensen, 2017; and Teddlie and Tashakkori, 2009.

FDA encourages researchers to consider the goals and objectives of using a mixed methods research approach and how the results from both qualitative and quantitative research components are intended to be used together.[22]

Reasons to use a mixed methods research design may include:

- Harmonizing and confirming results from different methods (triangulation)
- Supplementing and clarifying results from one method with results from another method (complementarity)
- Using results from one method to inform the design of another method
- Discovering inconsistencies, contradictions, and new perspectives, and reframing of questions or results from one method with questions or results from the other method (initiation)
- Expanding the scope (range) of a research question by using different methods for different components of the research question (expansion)

Questions researchers should ask to determine which mixed methods research approach to use to address their research question(s):

- Will qualitative or quantitative methods be more predominant in the study, or will both be given equal status (i.e., equal weight or equal priority) in the study?
- Should qualitative and quantitative components be carried out concurrently or sequentially?

With a mixed methods research approach, there is a possibility that the findings from the qualitative and quantitative components may appear to conflict with each other.[23] FDA encourages researchers to consider approaches that increase the understanding and interpretation of potentially conflicting findings. The selected approach should be guided by both the context and the research question(s).

VI. MANAGING BARRIERS TO SELF-REPORT

Typical techniques and/or methods to obtain self-report data may not be appropriate for all target populations and may need to be tailored to the population of interest. Consider the following approaches to obtain self-report data across broad populations:

- Participants with different capabilities (e.g., physical, sensory, intellectual, and/or communication)
  - Ensure usability of materials by participants with varying abilities or aids (e.g., low vision, tremor, using mobility aides).
    - Use written materials with large or adjustable font and that are screen reader accessible for respondents who are visually impaired.

[22] Johnson and Christensen, 2014.

[23] For additional information on how to address conflicting findings from mixed methods research, see Slonim-Nevo and Nevo, 2009.

    - Offer materials that can be read with a screen reader, or in an interview format, for those who cannot read.
    - Use instruction modification, infrared eye-trackers, and computerized tasks for people who are minimally verbal or nonverbal.

- Evaluation of the capabilities of people with intellectual disabilities through appropriate procedures or measurements to ensure they can validly provide their direct insights
    - Consider certain populations may have a limited attention span (e.g., young children).
    - Plan to conduct interviews in shorter segments.

- Pediatric populations
    - Ask young children to participate in drawing activities to help elicit concepts.
    - Use props.[24]

- Populations with caregivers
    - For respondents who have a caregiver, the caregiver generally should not be present during a patient interview (e.g., they may be asked to sit outside the room). In cases where it is important for the caregiver to be present with the patient (e.g., for patient comfort), the caregiver could sit behind the respondent to minimize influencing the interview (either verbally or nonverbally).[25] In either case, the research protocol should include a clear plan to document the presence and/or assistance of a caregiver and how data from the patient and caregiver will be collected and reported in these instances, so that the source of the information is clear for analysis and reporting.

For patients who are unable to self-report, eliciting what behaviors caregivers observe in the patients (including things the patients tell them) can help to avoid proxy reporting (i.e., reporting from the caregiver as if they were the patient).[26] Proxy reporting can lead to inappropriate inferences and may not be reflective of what a patient may be truly thinking or feeling.

Sometimes the barrier to self-report is language, dialect, or culture. Consider the following:

- Questions used in multicultural qualitative and quantitative studies should be culturally sensitive and use language that is adapted to the culture of interest to ensure appropriate responses.
- It is important to understand and consider how cultural differences may affect participant's responses.

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[24] For additional information on ***concept elicitation*** in children, see Matza et al., 2013.

[25] For additional information on considerations for including caregivers in qualitative interviews, see Matza et al., 2013.

[26] For more information on factors to consider when deciding the feasibility of self-report, see FDA guidance for industry *Patient-Focused Drug Development: Collecting Comprehensive and Representative Input* (June 2018).

- Poorly translated survey instruments can prevent researchers from collecting data comparable to that of surveys in the source (original) language.[27] Ideally, translatability assessment should be performed early during development of a survey instrument to address the needs of different nationalities, regions, and cultures.[28]
- In both qualitative and quantitative studies, translation and cultural adaptation procedures for multinational, multiregional, and/or multicultural survey studies should be used to keep the meaning of questions similar.
- In survey instruments, it is generally helpful to keep the format of the questions similar across translations, considering the differences among languages, and to retain the properties of the instrument, such as range of response options and scoring.

VII. CONSIDERATIONS FOR USE OF SOCIAL MEDIA

Social media may be an approach to collect qualitative and/or quantitative data:

- Data can be collected qualitatively through passive observation of social media discussions or information; observations can occur retrospectively or prospectively.
- Data can be collected prospectively by administering a survey instrument in a social media setting. Best practices for designing and implementing studies using survey instruments and technology also are applicable to the use of social media to conduct a survey.

Consider the following when using social media data:

- Choose an appropriate research design.
  - Mixed methods sequential research designs can further strengthen the depth of knowledge gained from social media data.
- Carefully select the source(s) of the social media with the research question in mind, because findings across social platforms may be distinctly different (e.g., certain platforms may have strong advocacy/support community presence; others may predominantly capture industry/academic perspectives surrounding certain issues).
  - Different social media communities appeal to different segments of the population, and the degree of a community's user anonymity may affect what users are willing to discuss. Research using social media data should examine a variety of social media networks and communities to obtain data that can be most generalized to the population of interest to the extent possible (i.e., generalizability).[29] A discussion of the strengths and limitations of using social media data in qualitative, quantitative, and mixed methods research can be found in Guidance 1.
- Use appropriate methods to collect and analyze data.

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[27] Survey Research Center, 2016; Wild et al., 2005.

[28] Further information on translation and culturable adaptation of survey instruments can be found in Acquadro et al., 2018; Survey Research Center, 2016; Wild et al., 2005.

[29] It is important to consider ethical standards (e.g., disclosure, consent, data ownership) for the collection and analysis of social media data, and any applicable federal, state, and institutional rules. For a discussion on ethical considerations, refer to Gleibs, 2014.

  - Data collection methods should address potential limitations (e.g., lacking mechanisms to verify patient characteristics, such as identity or diagnosis) and how these limitations can affect data integrity and interpretation.
- Assess data quality.
  - Verify content and sources to avoid false information (e.g., bots).
- Protect privacy.
  - Although verified patient community data may be used, in some cases, it may be appropriate to allow users to remain anonymous or post under a username (e.g., blogs and forums), particularly when topics are of a sensitive nature.

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Please note that the citation of a scientific reference in this guidance does not constitute FDA's endorsement of approaches or methods presented in that reference for any particular study. Study designs are evaluated on a case by case basis under applicable legal standards.

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APPENDIX 1. Other Qualitative Methods

In addition to one-on-one interviews and focus groups (refer to **section IIIA**), there are other qualitative methods that can be used to elicit what is important to patients, some of which are described in the following sections.

A. Delphi Methods

The Delphi Panel technique is a multistage survey process with the intent to achieve consensus among experts, which may include patients, on a topic or issue.[30]

B. Observational Methods

Observational research methods can involve observations of patients by the researcher in a naturalistic setting (e.g., home or school); a research facility; or virtual environment (e.g., online communities, social media) to generate data related to symptoms or daily life functioning. These methods often involve assessment of events, patient attitudes, and behaviors over a period of time. Observational methods might be used to help understand experiences described through other methods. Examples of scenarios where these methods could be useful include (but are not limited to):

- In-person observations of children with attention deficit hyperactivity disorder in a classroom setting
- Room surveillance live or through use of video recordings to capture behavior while sleeping
- Room surveillance for observation of aggressive behaviors or confusion in patients with advanced Alzheimer's disease
- Social media listening (e.g., observing interactions among social media users in an online community) to understand how patients with a disease or condition describe their experience with treatment

C. Facilitated Discussions at Patient Meetings

Facilitated discussions in well-organized public meetings that include patients, caregivers and patient representatives can generate useful public input and patient perspectives in specific disease/condition areas or topics. FDA has organized and led such meetings under its PFDD initiative. FDA also welcomes patient organizations to identify and organize patient-focused collaborations to generate public input on other disease/condition areas, using the process established by FDA-led PFDD meetings as a model.[31]

D. Survey Instruments with Open-Ended Questions

See section IV.

[30] There are many different Delphi methods described in the literature that can generate consensus data (Keeney et al., 2010).

[31] See https://www.fda.gov/drugs/developmentapprovalprocess/ucm579400.htm.

APPENDIX 2. Considerations for Selection of Qualitative Data Collection Methods

Table 4. Potential Strengths and Limitations of Qualitative Data Collection Methods

Data Collection Method	Strengths	Limitations
One-on-one interviews	• Can gain in-depth and broad information on the topic of interest, including nuanced data about an individual's experience and perspective • Can gain an understanding of how a respondent interprets a question that might be included in a questionnaire • Flexible format – can tailor interviews to generate appropriately detailed information based on research needs (e.g., through use of probing questions) • Greater scheduling flexibility compared with focus groups • Privacy and confidentiality – some people may be reluctant to share certain things in a group setting • Can be conducted in-person at a study site or at a person's home or via telephone or video conference	• Time-intensive (e.g., length of time it takes to conduct several patient interviews) • Participants may be uncomfortable providing complete or truthful information on sensitive topics to interviewers in person • Studies can be expensive (i.e., staff time for conducting multiple individual interviews and data analysis)
Focus groups	• Can gain in-depth information on the topic of interest as a whole • Flexible format (see above one-on-one interviews) • Efficiency – elicit feedback from multiple participants at one time • Participants can react to and build on each other's ideas • Relatively inexpensive	• May not be efficient in covering maximum depth on an issue for each individual • Participants may become distracted by other participants in the group • Participants may experience peer pressure within the group • Single individuals might dominate the conversation, preventing multiple perspectives from being shared • Group setting may inhibit some individuals from providing sensitive information • Participants may be uncomfortable with speaking in a group setting and/or public setting • Less flexibility in scheduling for a group of people, which can lead to recruitment challenges

Data Collection Method	Strengths	Limitations
Delphi panels	• May provide a method for reaching consensus among appropriate experts and stakeholders on important issues and topics • Anonymous[32] process, when appropriate, reduces the role of ego and interpersonal issues in reaching consensus • Information can be collected remotely (e.g., via email or file-sharing software) and at the convenience of the participant	• Lack of universal guidelines for process • Definitions of *expert* opinion are variable • No clear standards for acceptable level of consensus, which can make the Delphi process lengthy • Size of expert panel should be considered because it is difficult to achieve consensus among a larger group • Implications for lack of anonymity in the case of modified Delphi panel methods • Potentially high respondent burden if using a lengthy Delphi survey instrument • Can be time-consuming and costly (e.g., high key opinion leader remuneration costs)
Observations of patient behavior or events (e.g., ethnography studies, which may occur in real-world settings and in real-time; social media listening; videos)	• Opportunity to observe the participant's *experience* • May be low burden for participants because the observation does not require active participation • Potential to observe episodic behavior and signs in a real-world context • Observations do not rely on patient or caregiver report	• May be time-consuming and logistically cumbersome to execute if conducted in natural settings (e.g., study environments may vary across locations) • Patient and others' privacy needs to be addressed given patients will be observed in their daily lives • Some concepts and experiences are not observable • Can be expensive (e.g., equipment if recording behaviors, staff time for observing in real-time) • Participant behavior may be affected by observer presence • When conducted in naturalistic settings, variability among settings may affect the reliability and generalizability of the results

[32] Responses are anonymous only to group members; researchers are aware of respondent identities. Similar to the methods used in reporting aggregated data for interviews and focus groups, responses will be reported using a unique identifier assigned to each expert.

Data Collection Method	Strengths	Limitations
Facilitated discussions in organized patient conferences/meetings	• Gain in-depth information on the topic of interest • Efficiency – elicit feedback from multiple participants at one time • Can include real-time public polling exercises	• Input is limited to patients who can attend the meeting, which may affect the reliability and generalizability of the results • Although panelists speak to the moderator, participants do not interact with each other in the same way that focus group participants do • Representativeness and clinical confirmation of diagnosis may be difficult to determine • See the potential limitations of focus groups

APPENDIX 3. Study Materials for Qualitative Studies

Table 5 discusses considerations of special relevance to designing and implementing study materials for qualitative studies of patient experience.

Table 5. Study Materials[33]

Study Material	Components	Considerations
Research protocol	• Details on how the research will be conducted • Evidence to support the conduct of the study (e.g., unmet need) • Description of all research-related activities and study activities that patients will undergo	• Outline clear research objectives and questions; identify potential sources of bias • Specify details on target population, including demographics, clinical characteristics (e.g., phenotype, genotype, disease/condition severity), and other pertinent characteristics (e.g., geographic representation) – Use screening material to ensure the target population of interest is recruited • Specify how data will be prepared for analysis (e.g., transcription, audio-/video-recorded, internet data, metadata, archives) • Include information regarding projected clinical site enrollment characteristics (e.g., geographic location, referral/academic centers versus community centers) to help further characterize the study sample • See **Guidance 1** for details regarding considerations for study sampling and representativeness • Identify the number and duration of discussion sessions you plan to conduct; this should be dependent on: – Number of objectives and research questions – Demographic and cultural/linguistic diversity of the target population (e.g., by age, sex, gender, race, educational level), including number of subgroups (e.g., disease/condition severity levels, phenotypes, informants (just patients or patients and their caregivers))

[33] For the documents discussed in the table, there may also be other generally applicable regulations, guidance(s), standards and/or requirements.

Study Material	Components	Considerations
Interview/ discussion guide	• Interviewer/moderator instructions • Study instructions • Warm-up questions (e.g., questions to establish connection with participant) • Core topic-related questions • Wrap-up questions • Discussion conclusion	• Use terms participants can understand and avoid technical terms when possible (e.g., choose to use the term *shortness of breath* rather than *dyspnea*) • Avoid asking leading questions that guide participants to respond with a preferred answer • Avoid asking questions that imply you are casting judgment on a participant's beliefs or choices • Use open-ended questions rather than closed-ended questions, where appropriate, to elicit spontaneous information from participants – Probing questions may be appropriate based on the direction of the conversation (e.g., if patient misinterprets the question) • Frame questions within the context of a participant's experiences; avoid questions about abstract or theoretical concepts to the extent possible • Consider eliciting specific data by framing questions using targeted approaches such as: – Diary questions (patients asked to describe a typical day) – Critical incidents (patient reports worst/best experience) – Free listing (e.g., patients list all symptoms, impacts, treatments) – Ranking (e.g., patients rank importance of symptom, treatment benefit)
Training materials	• Detailed coverage of the research protocol contents • Consent/assent forms • Mock discussion session (staff can evaluate flow of discussion)	• Train staff using standardized training materials (e.g., training documents, slides) • Provide refresher training • Training on use of technology, where applicable • The consent/assent form should contain the appropriate information (i.e., elements of informed consent) • Train investigators/staff to present elements of informed consent/assent to prospective study participants and document the corresponding consent/assent
Glossary	• Definitions of terminology	• Clearly define key terminology within the text and ensure consistent terminology is used throughout study document(s)
Coding dictionary	• Codes (category or concept descriptions) • Coding structure	• Outline clear instructions for categorization, including code definitions, instructions, and considerations

Study Material	Components	Considerations
	• Memos (ideas or thoughts on how codes are derived))	• Derive initial codes from prior knowledge (e.g., natural history, conceptual model, disease model, discussion guide structure) • Develop a hierarchical organization of main codes and detailed codes
Data analysis plan	• Data to be collected • Analytic methods, including coding software • Identification of coders/analysts (including credentials) • Plans for resolving discrepancies among coders and other quality assurance measures (e.g., double-coding exercises) • Description of coding stages (e.g., initial coding, interim checks – including plans for coding dictionary refinement) • Plans for data visualization • Table/figure shells	• Should be established when planning a research study (i.e., before data collection begins) • Determine sample size needed for the study • Specify method for achieving and documenting saturation • Identify and specify appropriate analytic methods for data type • Identify analyses' assumptions • Consider approach most appropriate to present data (e.g., tables, figures)

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APPENDIX 4. Analysis of Qualitative Data

A. Data Preparation

Qualitative data can be voluminous, so it is important to have a standardized method to analyze and interpret the volume of data in a practical and consistent way. Qualitative data should be prepared before analysis. Preparation can include aggregation or transcription of data from different sources, including:

- In-person interviews or focus groups
- Recordings (e.g., audio, video, online)
- Internet (e.g., social media, chat room dialogues)
- Metadata (e.g., date of interview, name of interviewer, demographic details of respondent, source of field notes, initial ideas of analysis)

B. Data Analysis

Table 6 provides considerations for analyzing qualitative data. Note the steps for data analysis in qualitative studies may be iterative and are not necessarily sequential.

Table 6. Steps Typically Used for Data Analysis in Qualitative Studies

Steps	Description
Compiling and organizing data	• Arrange notes from research and other data collection in a useful and standardized order (electronic storage and computer programs)
Describing and classifying data	• Break down compiled data into smaller pieces • Reorganize pieces into different groupings/sequences (e.g., codes)
Interpreting data	• Use the grouped/sequenced data to identify the larger meaning of the data • Connect concepts from the data to other evidence (e.g., relevant literature, expert opinion) • Evaluate whether no new and important concepts have appeared (i.e., saturation) if applicable to the research objective
Representing and visualizing data	• Package data in a way that can be easily understood (e.g., text, tables, figures)

Transcripts should be analyzed using methods appropriate for categorization and aggregation of study results. There are different approaches to describe and classify qualitative data, some that may involve coding and some that may not. FDA generally recommends that qualitative data are coded for regulatory submissions.

If a coding approach is selected for analysis, considerations commonly include but are not limited to the following:

- Select the appropriate coding approach for the data of interest
- Determine the appropriate level of detail for what is to be coded (e.g., line-by-line coding or select segments of text)
- Decide what data is relevant enough to be coded
- Move methodically to a slightly higher conceptual level initially when coding data

- Carefully consider the grammatical form of the coded words to best summarize the basic topic of a passage of qualitative data (e.g., actions versus processes versus nouns)

When you have literature, expert input, and appropriate knowledge, a preliminary coding dictionary[34] can be developed. In many instances, codes are driven by the data; the coding dictionary will then evolve as new concepts are identified and emerge from the data. See the examples below.

EXAMPLES

Example 1

Coding line-by-line (applying codes to each line of qualitative data)

Fatigue Time-sensitive medication Interference with daily activities Limits physical functioning Rash Itchy	**01 INTERVIEWER** **02** *How do you feel when you take your* **03** *medicine?* **04 PATIENT** **05** *I feel extremely tired after taking my medicine. I* **06** *am not sure if it is related to the time of day that I* **07** *take it or not. Regardless, I cannot complete chores* **08** *around the house or take long walks.* **09** *I also have noticed a rash along my upper arm,* **10** *which has caused a lot of itching.*

Example 2

Using data to generate themes and codes

01 PATIENT **02** *Because I was in extreme pain, my doctor wanted to* **03** *re-evaluate some of my meds. The doctor told me I* **04** *would have to stay in the hospital for monitoring. I* **05** *was afraid that this was would not be covered under* **06** *my insurance. I ended up calling my family to see if* **07** *they could visit me.*	Pain Requesting regimen evaluation Hospitalization Medical access Family support

If a coding approach is not selected for analysis, methods that are commonly used include but are not limited to the following:

- Arrange notes (notes about original data) in a thematical manner
- Ensure your notes precisely cite the original data (or precisely locate the places in the database)
- Implement a procedural check (take notes and crosswalk them backwards into the original database)

It is important to note that regardless of analytic method, you should maintain a methodical analytical procedure to avoid nonsystematic and inconsistent judgments.

[34] A coding dictionary is a guide with predetermined concept categories and descriptions (related to the research objectives and questions) that is developed before data collection and analysis.

C. Saturation

When conducting iterative rounds of interviews, saturation is the point when no new relevant or important information emerges and collecting additional data will not likely add to the understanding of how patients perceive the concept of interest. Saturation is sometimes used in qualitative research as a principle for discontinuing data collection and/or analysis. However, the use of this principle will be dependent on the research objective. Although there are no set criteria or methodology for how saturation may be evaluated, the steps indicated in the example below is one approach.

EXAMPLE
Concepts reported in the first 25 percent of planned interviews with patients are compared to the next 25 percent of planned interviews after they are conducted. Both sets of interviews (50 percent of the originally planned number) are compared with the next 25 percent of the planned interviews, and subsequently all these interviews (75 percent) are compared to the next 25 percent of interviews. If saturation has not been reached by the initial planned sample size, or more information is needed in certain patient groups in order to fully assess saturation, more interviews may be needed. The goal of the saturation process is to compare the amount of new information that is observed in the first interview set to the second interview set and so forth. Interviews are typically conducted until saturation is met, and no new important concepts are emerging from the last set of interviews with a diverse group of patients.

Table 7 shows a saturation grid example summarizing focus group data. In this example, the researchers identified two symptoms (i.e., Symptom A and Symptom B) based on literature review and subject matter expert input. In addition, the researchers identified additional symptoms based on the transcripts (i.e., Other Emergent Symptoms). Before assuming that saturation may have been met, it is important to review focus group participant demographics to assess representativeness (i.e., do the focus group participants represent the intended target population as much as possible?).

Table 7. Saturation Table Example

Concept	Group 1	Group 2	Group 3	Group 4
Symptom A	5[1]	4	3	3
Symptom B	4[1]	3	5	3
Symptom C	3[1]	4	4	3
Symptom D		2[1]	1	2
Symptom E		3[1]	2	
Symptom F	4[1]	3	5	4
Symptom G			1[1]	

N=6 patients per focus group; 24 total patients
[1] Highlighted cells indicate the first time a concept is mentioned, and numbers within the cells indicate the number of patients in that focus group endorsing the concept.

D. Quality Control

To improve quality control of data, consider the following:

- Thoroughly read all qualitative transcripts and reread the transcripts
- Ensure codes are applied consistently to all data and apply quality assurance checks throughout the coding and analysis process
  - Have multiple coders (e.g., each coder recodes qualitative data more than once to ensure reliability)
  - Examine agreement among multiple coders to avoid inconsistent coding to the extent possible (e.g., a subset of data is coded by multiple coders using the same coding framework to examine the extent to which the data is coded in the same way)
- Document how data are collected and analyzed in a transparent manner (i.e., audit trail, memo to file)
- Analyze and summarize concepts emerging from the interviews in the order that data are collected (i.e., as interviews are conducted) and display in a table or grid

E. Data Reporting

Regarding reporting findings from qualitative studies, qualitative data should be presented in a clear manner. It is generally helpful to include participant statements, in the participants' own words, to represent the qualitative data. Stakeholders should use their best judgment on how best to present and/or report the data.[35]

[35] For more information on how to report qualitative data, see Tong et al., 2007; Gibbs, 2018, EQUATOR Network website and database (https://www.equator-network.org/reporting-guidelines-study-design/qualitative-research/).

APPENDIX 5. Screening and Exit Interview Studies/Survey Studies

Screening/exit interviews and survey instruments may be implemented within the context of a clinical study. They can be helpful in obtaining patient feedback regarding various topics, such as the following:

- Reported changes in symptoms or functioning (worsening/improvement/no change) experienced by patients throughout a trial; changes may be related to benefits, tolerability, and/or unintended effects
- Participant treatment expectations
- Anticipated and unanticipated symptoms and side effects
- Viability of proposed dosing regimen
- Patients' experience with clinical trial participation, for example:
  - In blinded studies, whether they thought they could tell they were on the experimental treatment (or not) and why they thought they were on that treatment
  - Thoughts regarding study procedures and study participation
  - Experience with methods of data collection (e.g., user experience with electronic data entry)
- Benefit-risk perspective(s) from the patient/caregiver

Screening/exit interviews and survey instruments can also be conducted with caregivers to obtain similar feedback on some of the above topics, if they are observable. Caregivers may have unique perspectives important for medical product development programs.

The following are examples of potential strengths associated with conducting screening/exit interviews and survey instruments:

- Contribute cumulative evidence on demographics, medical history, and aspects of the patient experience
- Inform initial development or refinement of a clinical outcome assessment in early medical product development through cognitive interviews as part of a mixed-method approach
- Add greater depth to data in rare diseases (or possibly other diseases or conditions with not much patient input) where stand-alone qualitative studies are less feasible
- Obtain participant input on meaningful outcomes and meaningful change by eliciting patient definitions of symptom improvement, stability, or worsening (this topic will be discussed further in other guidances)
- Provide information on trial integrity (e.g., whether blinding to treatment assignment was maintained)

Potential limitations of screening/exit interviews and survey instruments include:

- Extra burden on site staff (e.g., additional operational procedures beyond the clinical study)
- Extra burden for patients/caregivers, on top of standard clinical study protocol

- For interviews, issues might arise regarding interview scheduling, administration time and confidentiality (e.g., certain sites/countries cannot share participant contact details with third-party vendors who might be conducting the interviews)

If screening/exit interviews are implemented, FDA generally recommends a trained, neutral third-party interviewer to conduct the interviews. Interviews should generally be conducted before (i.e., screening interviews) or after (i.e., exit interviews) patients complete the main portion of the clinical study to avoid any potential compromise of study integrity.