
Patient-Focused Drug Development: Collecting Comprehensive and Representative Input Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

DRAFT GUIDANCE

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**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)**

**June 2018
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Patient-Focused Drug Development: Collecting Comprehensive and Representative Input Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

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1 **Patient-Focused Drug Development: Collective Comprehensive and**
2 **Representative Input**
3 **Guidance for Industry, Food and Drug Administration Staff, and**
4 **Other Stakeholders¹**
5

6
7 This draft guidance, when finalized, will represent the current thinking of the Food and Drug
8 Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not
9 binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the
10 applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible
11 for this guidance as listed on the title page.
12

13
14
15
16 **I. INTRODUCTION**

17
18 **A. Overview of the Series of FDA Guidance for Enhancing the Incorporation of**
19 **the Patient’s Voice in Drug² Development and Regulatory Decision Making**
20

21 This guidance (Guidance 1) is the first of a series of four methodological *patient-focused drug*
22 *development* (PFDD) guidance documents³ that FDA is developing to address, in a stepwise
23 manner, how stakeholders (patients, researchers, medical product developers and others) can
24 collect and submit *patient experience data*⁴ and other relevant information from patients and
25 caregivers for medical product⁵ development and regulatory decision making.
26

27 This series of guidance documents builds on learnings from the disease-specific PFDD meetings⁶
28 that FDA conducted under the fifth authorization of the Prescription Drug User Fee Act (PDUFA
29 V) as an enhancement of the Agency’s implementation of a more structured approach to *benefit-*

¹ This guidance has been prepared by the Office of New Drugs and the Office of Translational Sciences in the Center for Drug Evaluation and Research (CDER), in cooperation with the Center for Biologics Evaluation and Research (CBER), at the Food and Drug Administration.

² For the purposes of this guidance, all references to *drugs* include both human drugs and therapeutic biological products unless otherwise specified.

³ The four guidance documents that will be developed correspond to commitments under section I.J.1 associated with PDUFA VI under Title I of the 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. <https://www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm563618.pdf>

⁴ 21st Century Cures Act: <https://www.congress.gov/bill/114th-congress/house-bill/34>

⁵ A drug, biological product, or medical device.

⁶ <https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/ucm347317.htm>

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30 **risk assessment**.⁷ The PFDD meetings conducted to date have given FDA a deeper appreciation
31 for the expertise that patients and caregivers can bring to the process and the value of
32 incorporating their voice. This series of guidance documents is intended to facilitate the
33 advancement and use of systematic approaches to collect and use robust and meaningful patient
34 and caregiver input that can better inform medical product development and regulatory decision
35 making.

36
37 Focusing on practical approaches and methods, this series will inform stakeholders of FDA's
38 current thinking about methods that could be used bridge from important early-stage efforts to
39 gain patients' narrative perspectives on the clinical context (e.g., meetings with patients), to
40 development and use of **methodologically-sound** data collection tools in clinical trials. These
41 guidance documents will also address Agency expectations regarding what sort of analyses
42 might be conducted as part of this work and what sort of documents might be produced, and
43 when appropriate, submitted to FDA.

44
45 The topics and questions that each guidance document will address are described below.

46
47 **Guidance 1:** Whom do you get input from, and why? How do you collect the information?

48
49 *Guidance 1 will discuss sampling methods that could be used when planning to collect patient*
50 *input. It will also provide a general overview of the relationship between potential research*
51 *question(s) and method(s) when deciding from whom to get input (including defining the target*
52 *population and development of the sampling strategy).*

53
54 **Guidance 2:** What do you ask, and why? How do you ask non-leading questions that are well-
55 understood by a wide range of patients and others?

56
57 *Guidance 2 will discuss methods for eliciting information from individuals identified in*
58 *Guidance 1, gathering information about what aspects of symptoms, impacts of their disease,*
59 *and other issues are important to patients. It will discuss best practices in how to do qualitative*
60 *research including conducting interviews, development of interview guides, selection of types*
61 *of survey questions, and considerations for collecting demographics and survey information. It*
62 *will also discuss survey methods and qualitative research topics to help avoid misleading*
63 *results such as inadvertently priming patients in ways that can lead to results that poorly*
64 *represent what is important to patients.*

65
66 **Guidance 3:** How do you decide what to measure in a clinical trial and select or develop **fit-for-**
67 **purpose clinical outcome assessments (COAs)**?⁸

68
69 *Guidance 3 will address refining the list of important impacts and concepts from patients to*
70 *develop potential study instruments. Given that not everything identified as important by*
71 *patients, caregivers, and clinicians can demonstrate change in a specific treatment trial or is*

⁷ <https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/ucm326192.htm>

⁸ Words or phrases found in the Glossary appear in bold italics at first mention within the body of text in this document.

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72 *measurable, how will you select what to measure in a medical product development program to*
73 *show clinical benefit? How will you identify or develop fit-for-purpose COAs to assess*
74 *outcomes of importance to patients?*
75

76 **Guidance 4:** Once you have a COA measurement tool and a way to collect data using it, what is
77 an appropriate clinical trial endpoint?
78

79 *Guidance 4 will address topics related to COA-related endpoint development and*
80 *interpretation, including topics related to instrument administration and meaningful within-*
81 *patient score changes.*
82

83 This series will discuss methods and approaches for collecting information that can be applied
84 for different types of patient input. For example, in addition to work related to planning for use
85 of fit-for-purpose COAs, other research questions may include: What aspects of clinical trial
86 conduct (e.g., informed consent, oversight by an institutional review board (IRB), enrollment,
87 frequency of assessments, assessment burden, patient follow-up) can be better tailored to address
88 the needs and concerns of the patients? What steps can be taken to minimize patient burden due
89 to research participation? In all cases, the level of rigor of the methods and approaches applied
90 should be appropriate for the questions the study wants to address and the potential impact of
91 incomplete or misleading results.
92

93 The science of patient input is constantly evolving, and gathering robust and meaningful patient
94 experience data to inform medical product development is a collaborative process. This
95 document is intended to serve as a basis for dialogue. Stakeholders around the world have
96 developed and are developing templates, checklists, and guidelines for different aspects of
97 gathering and interpreting patient experience data. As these projects and documents mature, we
98 will be updating our approaches. If you are considering collecting patient experience data, FDA
99 encourages you to have early interactions with FDA and obtain feedback from the relevant FDA
100 review division on appropriate research design.
101

102 In general, FDA's guidance documents do not establish legally enforceable responsibilities.
103 Instead, guidances describe the Agency's current thinking on a topic and should be viewed only
104 as recommendations, unless specific regulatory or statutory requirements are cited. The use of
105 the word *should* in Agency guidances means that something is suggested or recommended, but
106 not required.
107

B. Purpose and Scope of Guidance 1

108 The purpose of Guidance 1 is to present sampling methods for collecting information on the
109 patient experience that is representative of the intended population to inform the development
110 and evaluation of medical products throughout the medical product lifecycle. In addition, this
111 document discusses methods on how to operationalize and standardize the collection, analysis,
112 and dissemination of patient experience data.
113
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116 Hypothetical case examples, which provide practical supplemental information that illustrate
117 important concepts presented in this guidance, will be posted on the [CDER PFDD webpage](#).⁹
118

119 Guidance 1 also includes a glossary of terms that will be used in one or more of the four
120 guidance documents¹⁰.

121
122 In addition to standardizing terminology for an identified disease area, the information in
123 Guidance 1 should help the user develop a plan that will:

- 124 • Identify approaches and methods to collect information from patients and caregivers
- 125 • Identify approaches to sampling will ensure that the input to be collected is sufficiently
126 representative of the range of clinically relevant diversity in the patient population
- 127 • Identify methods and necessary steps to develop a plan for analysis and reporting of the
128 information that will be collected
- 129
- 130
- 131
- 132

133 The level of rigor needed for generating patient experience data can vary across studies and will
134 depend on the intended use. However, there are certain common elements to all studies such as a
135 protocol, structured data collection, and analysis.

136
137 This document is intended to serve as a focus for continued discussion among FDA, patient
138 partners, medical product developers, researchers, and others.¹¹ It is anticipated that this
139 document will provide a foundation for FDA and external stakeholders in the development of
140 subsequent relevant guidance(s) on patient-focused medical product development. Although this
141 document presents methods and approaches for collecting patient experience data, it does not
142 fully address methods for collecting and analyzing COAs or ***patient preference information***.
143 Some of those issues are addressed in the following guidance for industry¹²:

- 144 • *Patient-Reported Outcome Measures: Use in Medical Product Development to Support*
145 *Labeling Claims*
- 146 • *Patient Preference Information—Voluntary Submission, Review in Premarket Approval*
147 *Applications, Humanitarian Device Exemption Applications, and De Novo Requests, and*
148 *Inclusion in Decision Summaries and Device Labeling.*
- 149
- 150
- 151

152 If you are considering collecting patient experience data, FDA encourages you to have early
153 interactions with FDA and obtain feedback from the relevant FDA review division.

⁹ <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm579400.htm>.

¹⁰ The draft glossary of terms has been shared as an attachment to this guidance.

¹¹ In addition to consulting guidances, stakeholders are encouraged to contact the appropriate FDA office to discuss specific issues that arise during drug development.

¹² 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>.

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C. Patient Experience Data

What is patient experience data? Patient experience data is defined in Title III, section 3001 of the 21st Century Cures Act (Pub. L. 114-255), as amended by section 605 of the FDA Reauthorization Act of 2017 (Pub. L. 115-52) (FDARA), to include data intended to provide information about patients’ experiences with a disease or condition, including the impact (including physical and psychosocial impacts) of a disease or condition, or a related therapy or clinical investigation on patients’ lives; and patient preferences with respect to treatment of their disease or condition.¹³ Patient experience data can be understood as including (but is not limited to) the experiences, perspectives, needs and priorities of patients related to:

- the symptoms of their condition and its natural history;
- the impact of the condition on their functioning and quality of life;
- their experience with treatments;
- input on which outcomes are important to them;
- patient preferences for outcomes and treatments; and
- the relative importance of any of these issues 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 (McCarthy *et al.*, 2016; Wolf, Niederhauser, Marshburn, & LaVela, 2014).

The patient’s journey should be defined from the patient perspective. An understanding of that perspective may be enriched or 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.*, 2018). [Table 1](#) describes types of patient partners.

¹³ The definition is codified at section 569C(c)(4) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), and applies to section 3002 of the 21st Century Cures Act, which directed FDA to issue certain guidance documents regarding the collection of patient experience data, see section 3002(b).

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187 **Table 1. Types of Patient Partners**

188

- 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 advocate** is an individual or group that advocates for patients’ health or healthcare. The advocate may or may not be part of the target population, and may work to influence healthcare policies or practices.

189

190

191 There are different parts of the patient experience to collect and/or measure in medical product
192 development, which may include but are not limited to:

193

194 • Impact of the disease and its treatment on the patient

195

196 ○ signs/symptoms of disease or condition

197 ○ chief complaints (most bothersome signs/symptoms)

198 ○ burden of living with a disease or condition

199 ○ burden of managing a disease or condition

200 ○ burden of participating in clinical studies

201 ○ impacts from disease or condition on activities of daily living and functioning

202 ○ impacts from treatment on activities of daily living and functioning

203

204 • Patients’ perspectives about potential and current treatments

205

206 ○ minimum expectations of benefits

207 ○ tolerance for harms or risks

208 ○ acceptable tradeoffs of benefits and risks (i.e., patient preference)

209 ○ attitudes towards uncertainty

210

211 • Views on unmet medical needs and currently available treatment options

212

213 • Enhanced understanding of the natural history of the disease or condition, including
214 progression, severity, chronicity

215

216 Information collected on patient experience will be referred herein as patient experience data.

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218 ***Can data be collected from other experts as well?*** Where appropriate to supplement patient
219 experience data, FDA recommends also gathering input from clinicians and other experts in the
220 given disease area to ensure important clinical outcomes are studied.

221
222 ***Who can collect and submit patient experience data?*** Patient experience data can be collected
223 by any persons including (but not limited to): patients, family members and caregivers of
224 patients, patient advocacy organizations, disease research foundations, researchers, and drug
225 manufacturers. It should be clear in any submission to FDA which person or group has collected
226 the data.

227
228 ***Why is it important to collect patient experience data?*** Patients are experts in their own
229 experience of their disease or condition and the ultimate consumers of medical products. The
230 collection of patient experience data is important because it provides an opportunity to inform
231 medical product development and enhance regulatory decision making to better address patients'
232 needs.

233
234 ***When do you collect patient experience data?*** Patient experience data may be collected
235 throughout medical product development, beginning early in development (e.g., discovery) or
236 independent of any specific medical product development program (precompetitive setting).
237 Patient experience data can be used to help identify unmet medical needs and important clinical
238 outcomes to be studied, as well as inform the design of future clinical trials. Further, patient
239 experience data can help inform COA development and selection, as well as analyses and
240 communication of benefit-risk.

241
242 ***When should patient stakeholders be involved in product development?*** Patients (including
243 patients serving as advisors) should be meaningfully involved throughout the medical product
244 development process—not only as study subjects but as partners. Engaging patients actively in
245 the development process can potentially improve rates of trial enrollment and retention and
246 increase applicability to patients (Bower *et al.*, 2014).

247
248 ***How do you collect patient experience data?*** Qualitative, quantitative, or mixed methods may
249 be appropriate to collect robust and meaningful patient experience data depending on study goals
250 and the research questions. These methodological approaches are discussed in [Section III](#) of this
251 document and [Appendix 1](#). Some general distinctions between each method are shown in [Table](#)
252 [2](#). Factors to consider when selecting an appropriate methodological approach are discussed in
253 [Section II](#).

254
255 Patient experience data can be collected in a variety of research contexts, including (but not
256 limited to): clinical trials, observational studies, advisory boards, public meetings, and other
257 novel settings (e.g., online patient communities). The level of rigor needed for patient experience
258 data generation can vary across studies and will depend on the intended use. As such, it is
259 important to begin discussions with FDA early to determine which approach should be used.
260 Methods for generating patient experience data will be discussed in more depth in Guidance 2.

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262 **Table 2. Methodological Distinctions for Collecting Patient Experience Data**

263

Research Approaches			
	Qualitative Research	Quantitative Research	Mixed Methods Research
<i>Common Research Objectives</i>	<ul style="list-style-type: none"> • Description, understanding, and exploration/confirmation 	<ul style="list-style-type: none"> • Numerical description, causal explanation, and prediction 	<ul style="list-style-type: none"> • Multiple objectives; provide complex and fuller explanation and understanding; understand multiple perspectives
<i>Common Study Characteristics</i>	<ul style="list-style-type: none"> • Attempt to understand participant views, perspectives and meanings of concepts; study groups and individuals in natural or controlled settings 	<ul style="list-style-type: none"> • Study behavior under controlled conditions; isolate the causal effect of single variables 	<ul style="list-style-type: none"> • Study multiple contexts, perspectives, or conditions; study multiple factors as they operate together
<i>Data Collection</i>	<ul style="list-style-type: none"> • Qualitative data such as in-depth interviews, participant observations, field notes, and open-ended questions 	<ul style="list-style-type: none"> • Quantitative data generated using structured data-collection instruments 	<ul style="list-style-type: none"> • Both qualitative and quantitative data
<i>Data Characteristics</i>	<ul style="list-style-type: none"> • Words, images, categorizations 	<ul style="list-style-type: none"> • Quantifiable variables 	<ul style="list-style-type: none"> • Mixture of quantifiable variables, words, categorizations, and images
<i>Data Analysis</i>	<ul style="list-style-type: none"> • Use descriptive analysis to identify patterns, themes, and holistic features of qualitative data 	<ul style="list-style-type: none"> • Identify statistical relationships among variables 	<ul style="list-style-type: none"> • Quantitative and qualitative analysis used separately and in combination
<i>Examples</i>	<ul style="list-style-type: none"> • A group of patients are interviewed to describe their experience with the disease or condition 	<ul style="list-style-type: none"> • A group of patients are surveyed about their experience with the disease or condition symptoms with a questionnaire that uses closed-ended questions with distinct response options to quantify information 	<ul style="list-style-type: none"> • A group of patients are given a survey or questionnaire with both open-ended and closed-ended questions

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264 ***How can external stakeholders submit patient experience data to FDA?*** It is important to
265 remember that patient experience data informs development and evaluation of medical products
266 throughout the medical product lifecycle. There are various pathways to (a) submit patient
267 experience data to FDA and (b) engage with FDA for discussion. Additional FDA guidance on
268 how to submit patient experience data is under development. Depending on the type of patient
269 experience data and the intended purpose of the data with respect to medical product
270 development, different content and formats may be appropriate for submission. At the minimum,
271 when patient experience data are submitted to the agency, a study report and protocol from the
272 research study should be submitted to FDA, as well as additional information including the
273 primary data capture (see [Section IV](#) and [Appendix 2](#)).

274
275 Specific criteria defining what is most informative and useful for FDA submission should be
276 discussed early with the appropriate FDA review division(s), as the level and type of criteria
277 might vary based on how the data will be used. However, in all cases the intended purpose of the
278 patient experience data being submitted to the Agency (i.e., how the data are intended for use in
279 supporting medical product development and regulatory decision making) should be made clear
280 in the submission.

281
282 Many existing FDA regulations, guidances, and other standards and requirements pertaining to
283 the capture/collection, transmission, processing, storage, archiving, retention, and submission of
284 data from clinical studies conducted to support a regulatory medical product application (e.g., an
285 investigational new drug application (IND), new drug application (NDA), or biologics license
286 application (BLA) or medical product labeling language also apply to patient experience data
287 generated in such studies. See [Appendix 2](#) for a partial list of such regulations, guidance(s),
288 standards, and requirements.

289
290 ***How is patient experience data used for regulatory purposes?*** Patient experience data is used to
291 help inform clinical trial design, trial endpoint selection, and regulatory reviews including
292 benefit-risk assessments as well as potential labeling (or other communications). FDA
293 encourages stakeholders considering collecting and submitting patient experience data to FDA to
294 have early interactions with FDA during the design phase of such studies and obtain feedback
295 from the relevant FDA review division.

296
297 FDA values the use of patient input to help foster the development and availability of safe and
298 effective medical products. The collection of patient input helps FDA gain a better understanding
299 of the patient experience and expected clinical benefit.

300 301 **II. GENERAL CONSIDERATIONS FOR COLLECTING PATIENT EXPERIENCE** 302 **DATA**

303 304 **A. Overview**

305
306 The selection of people from whom to collect input depends upon the specific questions and
307 issues to be addressed. Thus, the selection process starts by considering the research question:
308 what are the specific objectives to be addressed by collecting patient input? Are the objectives

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309 focused on understanding the most burdensome symptoms, the impact of current therapies, their
310 tolerance for risk, or the course of the disease over time? Each of these may require different
311 approaches to patient selection and input collection.

312
313 ***How do you select a research approach?*** The research approach should be determined during
314 the study design phase, prior to study implementation, and should be comprised of the plans for
315 your research as well as the steps to implement those plans. While selecting the appropriate study
316 methods, you should consider the broad research assumptions underlying your study design as
317 well as the detailed elements that should be incorporated into the methodology to meet those
318 assumptions and achieve success (Johnson & Christensen, 2017; Teherani, Martimianakis,
319 Stenfors-Hayes, Wadhwa, & Varpio, 2015).

320
321 Some factors that are important to consider when selecting a research approach include:

- 322
- 323 • Research goals or questions to be addressed
 - 324
 - 325 • Target population and availability of people in that population
 - 326
 - 327 • Most valuable information that should be generated through the study to achieve your
328 research goals or answer your questions
 - 329
 - 330 • Expected short-term and long-term impacts of the information you intend to gather
331 through the study
 - 332
 - 333 • Amount of time to conduct your studies
 - 334
 - 335 • Study budget (including staffing, travel time, facilities costs, remuneration, data storage,
336 management, and analysis)
 - 337

338 If the research objective changes within the study, the research approach should be adjusted
339 accordingly. You may leverage and build upon existing literature and data to fit the specific
340 needs of the research question(s) (See [Section II.F.3](#)).

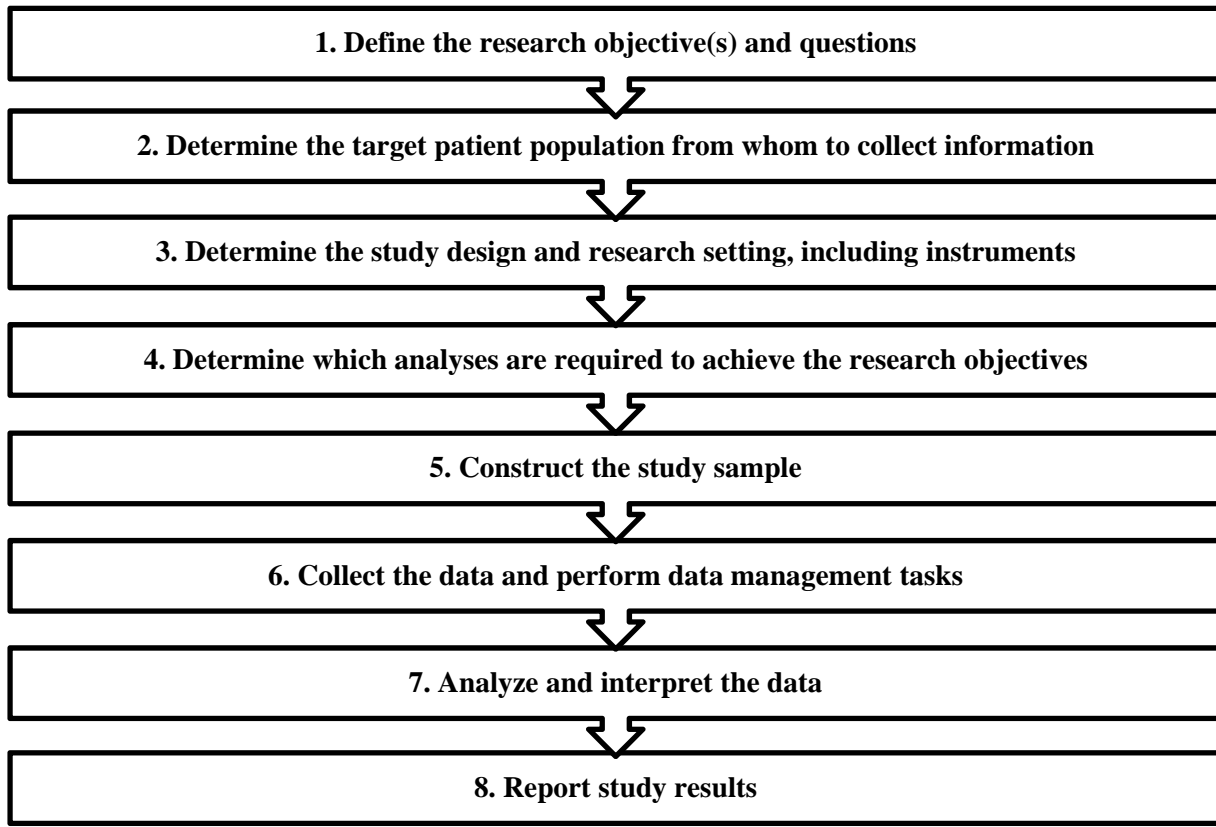
341
342 ***What steps should be used to collect patient experience data?*** FDA generally recommends that
343 stakeholders follow the general steps listed in [Figure 1](#) for studying patient experience to the
344 extent possible. The subsequent sections provide additional details.

345
346 **Figure 1. General Steps for Conducting Studies about Patient Experience**

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B. Defining the Research Objectives and Questions

How do you define research objectives and questions? In general, your research objectives are defined by the research questions you are trying to answer. When formulating your research objectives, you should be specific. It may be useful to break down a broader research goal into specific research objectives 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 along with subject matter experts (e.g., clinicians, social scientists). This will help to determine the most appropriate questions that will guide your study procedures. 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).

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Example:

Research objective: To explore the attitudes toward treatment of U.S. teenage patients with human immunodeficiency virus (HIV)

Research questions:

1. How does HIV treatment impact patients' daily lives?
2. Why might HIV patients not use certain treatments?
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 or answering questions or sharing concerns about living with HIV, it might be more suitable to engage them in one-on-one interviews over the telephone or other methods to provide them with a more comfortable interview setting rather than in group discussions or even administering a survey.

C. Who to Collect Information From

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 including the data collection mode that you choose for your study. It is important to tie the target population characteristics to the study sample and inclusion criteria. It also is useful to talk with FDA about how the target population could inform future medical product development and regulatory decision making.

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. However, more restrictive patient inclusion criteria (e.g., limiting patients to specific geographic regions), the less likely it is the information is generalizable to a broader sample. PD patients in California may have different views and preferences than those in another country or even another part of the US.

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, unless the patient cannot reasonably be expected to reliably self-report (e.g., young children, individuals with cognitive problems, such as Alzheimer's disease). In such cases, a clinician or other trained health care professional and/or

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416 primary caregivers, may report on patient experience if it is observable (e.g., signs of disease or
417 condition, functioning) (FDA, 2015). Patient partners can also provide valuable information
418 about the patient experience.

419
420 The **reporter** (the person who will be providing the patient experience information) may vary
421 from patient to patient within the target population.

422
423 Factors to consider when deciding if self-report is feasible include but are not limited to:

- 424
- 425 • Age
 - 426 • Level of cognitive development or function
 - 427 • Communication (e.g. linguistic, numeracy) skills
 - 428 • **Health literacy** (including basic **literacy**)
 - 429 • Insight
 - 430 • Health state
 - 431 • Co-morbidities

432
433 Prior to study initiation, it is important to set the criteria for determining the reporter. This may
434 include, for example,

- 435
- 436 • What is the minimal age limit at which children can provide reliable information?
 - 437
 - 438 • What is the minimal cognitive function at which individuals can provide reliable
439 responses?
 - 440
 - 441 • What are the scenarios under which multiple reporters may be required?

442
443 The reporter should be recorded for each individual in your study.

444

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

449
450 FDA recommends stakeholders engage with subject matter experts (e.g., clinicians, social
451 scientists) in the specific disease area of interest when determining the appropriateness of self-
452 report in the target population.

453 3. *Subgroups*

454
455 All subgroups of interest should be pre-specified at the study design stage whenever possible.
456 Care should be taken with the number of subgroups being proposed for analysis and inference.
457 Subgroups of interest may be based on reporter type (e.g., patients versus primary caregivers)
458 and/or socioeconomic, demographic, cultural, linguistic, clinical, or other factors pertinent to the
459 disease/condition of interest.
460

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461 **D. Determining the Study Design and Research Setting**

462

463 *How do you determine the research study design and setting?*

464

465 Some study features that are important to consider when determining your research study design
466 and setting include:

467

- 468 • Study Type (e.g., a clinical trial/study, observational study, survey study)
- 469 • Methodological Approach (e.g., qualitative, quantitative, or mixed methods)
- 470 • Sampling Method
- 471 • Including sample size
- 472 • Patient Selection
- 473 • Including methods for diagnosis determination (e.g. self-report, clinician report, other
474 source)
- 475 • Subgroups
- 476 • Whether special considerations are needed for subgroups of interest

477

478 In general, these study features are determined by your research objectives and questions, and to
479 some extent, they are determined by your resource constraints.

480

481 1. *Sampling Methods*

482

483 Prior to eliciting patient experience data, it is important to determine how individuals are to be
484 selected to participate in your study. This is sometimes referred to in the statistical literature as
485 the sampling scheme. Understanding how patients are sampled into your study determines
486 whether your research objectives and questions can be answered by the patient experience data
487 that you will collect.

488

489 There are many sampling approaches, each varying in complexity, the use of which depends on
490 your research objectives and resource constraints. FDA recommends stakeholders engage with
491 subject matter experts (e.g., statisticians, psychometricians) when determining the
492 appropriateness of sampling methods to use.

493

494 **Table 3** provides a listing of sampling approaches that are used to obtain patient experience data.
495 They can be classified under two broad categories:

496

- 497 • probability and
- 498 • non-probability.

499

500 **Example:** If you intend to conduct a study that is exploratory or hypothesis generating, with a
501 view towards gaining insight into patient experience (see Section III.A), then a non-probability
502 sampling approach may suffice. See Table 3 for the different types of non-probability sampling
503 approaches.

504

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506 The necessary components for probability sampling include:

507

- 508 • Well-defined target population
- 509 • Listing of individuals within the target population
- 510 • Random device such as a random number generator

511

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

517

518 **Example:** Suppose the target population consists of 100,000 Parkinson’s disease (PD) patients
519 alive in the US and each individual is enumerated in a sampling frame with a label of 1 to
520 100,000. A sample of 2000 patients is randomly selected from among the 100,000 patients and
521 their experiences are ascertained. Random sampling provides a mechanism for extending
522 statements made about patient experience based on the individuals in the sample to the entire PD
523 population. In practice, note that additional steps such as stratification may be needed to induce a
524 sample having the desired characteristics.

525

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

530

531 It is beyond the scope of this document to discuss these sampling schemes in any detail.
532 However, more in-depth discussions with respect to advantages and disadvantages can be found
533 in the literature (For example, Fricker, 2008; Groves *et al.*, 2009; Heckathorn, 1997; Johnson &
534 Christensen, 2014; Johnson, 2015; Korn & Graubard, 1999; Levy & Lemeshow, 2013;
535 Rothenberg, 1995; Valliant, Dever, & Kreuter, 2013).

536

537 As noted earlier, the appropriate sampling scheme is that which

538

- 539 • enables you to answer your research objectives and questions, and
- 540 • can be implemented within the scope of your resource constraints.

541

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543 **Table 3. Types of sampling, examples, and some potential limitations**

544

Types of Sampling	Selection Strategy	Examples	Potential 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.	<ul style="list-style-type: none"> • Can be expensive or infeasible to conduct. • SRS samples can fail to 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.	<ul style="list-style-type: none"> • 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)	<ul style="list-style-type: none"> • The initial probability sampling phase may not be feasible. • Relies on the initial respondents to identify members in their network.

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Types of Sampling	Selection Strategy	Examples	Potential Limitations
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.	<ul style="list-style-type: none"> • Often requires information about cluster size as selection probabilities can depend on such information. • 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. <ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • Often requires information about cluster size as selection probabilities can depend on such information. • Units within cluster tend to be homogeneous.
Non-Probability Sampling			
Clinical Trials	A sample that consists of patients who volunteer to participate in a clinical trial.	Patients with iron deficiency anemia are recruited to participate in a clinical study that compares the efficacy of an experimental therapy against a standard of care.	<ul style="list-style-type: none"> • Trial results may not be generalizable to the population of all iron deficiency anemia patients for whom the therapy is indicated.
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	<ul style="list-style-type: none"> • Study results may not be generalizable to the target population.

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Types of Sampling	Selection Strategy	Examples	Potential Limitations
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 and selects their sample based on these characteristics (i.e., adult females with acne) and objective of study.	<ul style="list-style-type: none"> • Study results may not be generalizable to the target population.
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.	<ul style="list-style-type: none"> • Study results may not be generalizable to the 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.	A convenience sample of individuals with substance use disorders (SUDs) is recruited. Each individual in this initial sample is provided a fixed number of coupons which he/she uses to recruit others in his/her network. The 2nd set of individuals recruited via coupons by the first set of individuals are also given a fixed number of coupons which they use to recruit individuals in their network. This is repeated for a fixed number of cycles after which recruitment terminates. The coupons serve as financial incentives for the recruited to	<ul style="list-style-type: none"> • Requires long recruitment chain and socially-networked population. • Study results may not be generalizable to the target population unless assumptions, which are not verifiable, are valid.

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Types of Sampling	Selection Strategy	Examples	Potential Limitations
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.	recruit others in the network. 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.	<ul style="list-style-type: none"> • Study results may not be generalizable to the target population.
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	<ul style="list-style-type: none"> • Limited by pre-registered panelists • Study results may not be generalizable to the target population. • Potential response bias (e.g., measurement error, misclassification)

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2. Representativeness

What is representativeness? When studying patient experience, it is important to obtain patient experience data that are not only relevant, objective, and accurate, but also representative of the target population. This is because it is usually impractical or impossible to select or study all patients in your target population. In this document, the term *representative* or *representativeness* can be interpreted in the following ways.

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554 (1) **A sample is representative of the target population if statements made about patient**
555 **experience based on data from the sample of patients are generalizable to the target**
556 **population.** In principle, probability sampling schemes enable you to obtain such
557 representative samples and often arise in the context of quantitative studies. However, if
558 there are subgroups of patients from the target population that are not adequately
559 represented in your study sample, your ability to generalize your research findings to the
560 target population may be limited, even if you use a probability sampling scheme.

561
562 (2) **A sample is representative of the target population to the extent that patients in the**
563 **study sample consists of individuals of various characteristics that to some degree**
564 **approximate the heterogeneity of characteristics in the target population.** For
565 example, your sample might consist of individuals from all levels of disease severity but
566 the severity distribution in your sample does not necessarily resemble the severity
567 distribution in your target population. This implies that statements made about patient
568 experience based on data from the study are not necessarily generalizable to the target
569 population. Whether this is acceptable depends on the research objectives. If your
570 research objective is concept elicitation or hypothesis generation or instrument
571 development, then this interpretation of representativeness is sufficient.

572 573 3. *Sample Size*

574
575 Sample size estimates are driven by:

- 576 • research objectives
- 577 • type of outcomes/endpoints under consideration
- 578 • study design
- 579 • planned methods of analysis
- 580 • whether the study is quantitative or qualitative in nature.

581
582
583 Having an insufficient sample size may produce unreliable and/or imprecise results. FDA
584 recommends that if the sample size is limited due to practical considerations (e.g., rare diseases),
585 the research objectives should be adjusted accordingly and noted as a limitation in the study
586 report. Other practical considerations include:

- 587 • Small amounts of data

588
589
590 The number of sampled individuals completing the study may be small. In this case, or
591 when missing data/non-response are impactful, estimated sample size may need to be
592 adjusted upward to maintain the desired level of statistical information.

- 593 • Subpopulations of interest

594
595
596 There may be specific interest in one or more subpopulations. In this case, the sample
597 size should be determined to ensure there is sufficient information to make statements
598 about the subpopulation of the target population. If the goal of the study emphasizes both

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599 the target population and a subpopulation within the target population, then the sample
600 size should be determined to ensure that there is sufficient information to make
601 statements about the subpopulation and the target population.

602

- 603 • Study design and analysis sample size needs

604

605 The appropriate analysis methods for a study design may be unstable at certain sample
606 sizes. Sample size calculations should take these features into consideration.

607

608 a. Studies Using Qualitative Methods

609

610 For qualitative studies, sample size determination is often less formal and based on the concept
611 of saturation, which roughly means no new relevant or important information (e.g., new concepts
612 of importance and relevance to subjects and research question) is gained by recruiting additional
613 patients (Dworkin, 2012; Francis *et al.*, 2010) and the group of patients thus far recruited appears
614 to be representative. As such, sample size formulae for such studies are often unavailable.

615 Although sample size determination for qualitative studies is usually subjective, there is some
616 guidance in the literature (Dworkin, 2012; Francis *et al.*, 2010; Sandelowski, 1995).

617

618 b. Studies Using Quantitative Methods

619

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

621

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%).

622

623 For studies focusing on a single population, sample size calculation may be based on a precision
624 criterion. For example, a study may require a sample size that is sufficiently large such that the
625 estimated prevalence has a margin of error of at most 5% (roughly, precise to within 5%).

626 Sample size calculations for different sampling types, study types, and data types can be found in
627 the literature (Chow, Wang, & Shao, 2008; Levy & Lemeshow, 2013; Thompson, 1987). For
628 complex designs where sample size formulae are intractable to obtain, simulation could be used.

629

630 E. Constructing a Sampling Frame

631

632 The existence of a sampling frame facilitates probability sampling. Without a sampling frame, it
633 is potentially difficult or infeasible to randomly sample from the target population. To the extent
634 that disease registries are inclusive and regularly-updated, they may provide a natural sampling
635 frame. The scope of registries may vary, with some defined at the

636

- 637 • national level

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- 638 • state level
- 639 • some local to an organization such as a hospital or a chain of hospitals owned by a
- 640 particular organization or part of a network.

641
642 For many disease areas, however, registries may not exist or may not be inclusive or well-
643 maintained. In such cases, resources may have to be devoted to constructing the sampling frame.
644

Example: In the United States, physician listings such as the AMA Masterfile or state licensing board files have 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.

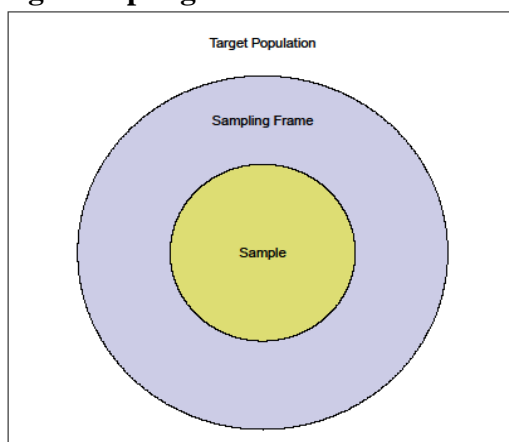
It is important to note that unless all physicians treating patients are sampled, and all relevant patients under the care of each physician are identified, the resulting sampling frame may exhibit undercoverage in the sense that not every member of the target population is counted in the frame.

645
646 **Figure 2** illustrates the concept of undercoverage. The target population of interest is depicted as
647 the outer square. Undercoverage occurs because a proportion of members of the target
648 population is not included in the sampling frame, the large circle. In general, undercoverage may
649 not be problematic if:

- 650
- 651 • members excluded from the frame could be reasonably viewed as not being substantially
652 different from those enumerated in the frame, and
- 653 • the primary goal of the study is to understand the distribution of the patient experience in
654 the target population, rather than to estimate total number of people.

655
656 Regardless, attempts should be made to minimize undercoverage so that the patient population in
657 the frame is not substantially different from the target patient population. In some cases, it may
658 be possible to conduct a screening study to identify members of the target population and create
659 a sampling frame.

660
661 **Figure 2. Example Undercoverage Sampling Frame**



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663 F. Additional Considerations

664

665 1. Sufficient Representation

666

667 For research questions in which probability sampling is appropriate, it might be possible to
668 achieve sufficient representation through careful construction of a sampling frame, and selection
669 and implementation of an appropriate probability sampling scheme.

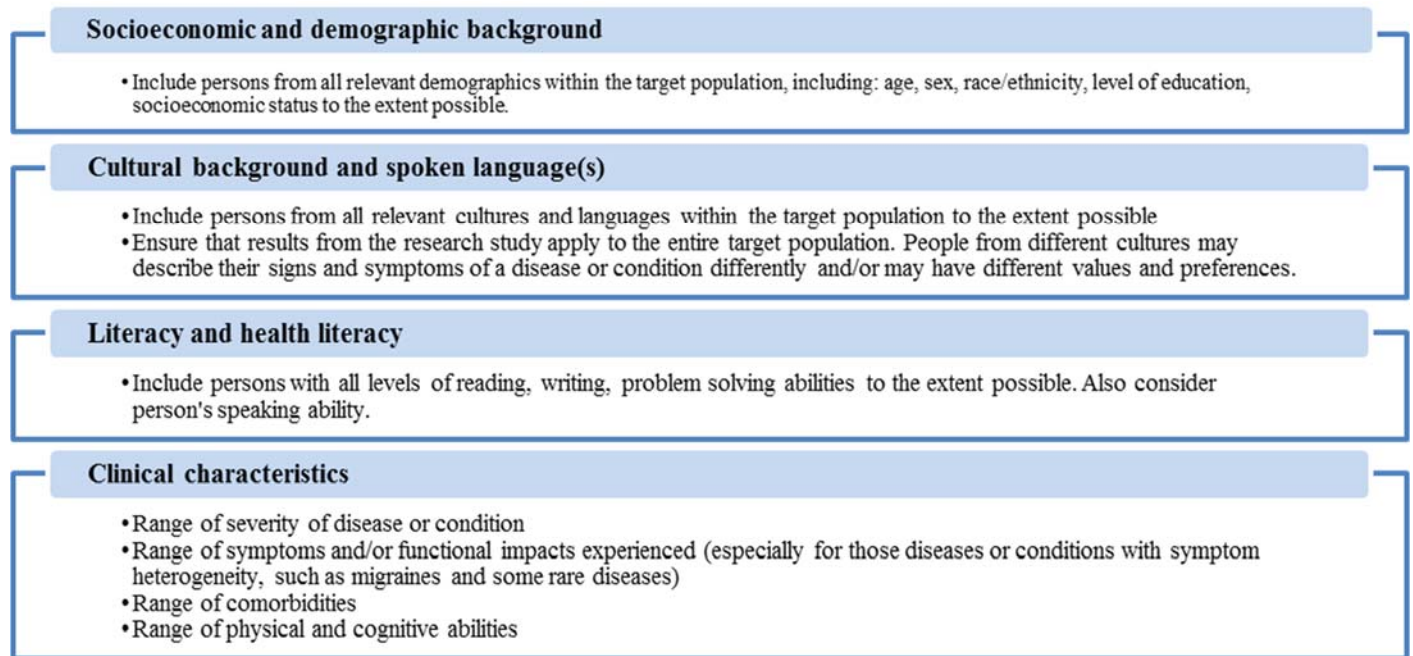
670

671 However, there are scenarios in which probability sampling may not be feasible or required.
672 Regardless of how individuals are selected into the study, it is important to ensure that patients in
673 the study sample represent the target population, to the greatest extent possible, particularly with
674 respect to the attributes that are associated with the endpoints of interest. For example, in a study
675 of patients with a specified condition, to the extent that patients who have multiple comorbidity
676 conditions may have patient experience distributions that are different than those with few or no
677 comorbidity conditions, it is important that patients of varying levels of comorbidities are
678 selected for your study. [Figure 3](#) provides some guidance regarding factors to consider to
679 achieve sufficient representation.

680

681 **Figure 3. Factors to Consider to Achieve Sufficient Representation**

682



683

684

685 2. Missing Data/Non-response

686

687 Missing data is common in most types of studies. In randomized studies for example, some
688 individuals may withdraw from the study prior to study completion. In observational
689 epidemiological studies using electronic health records, some information that is important to the
690 determination of a safety question was not collected by some health care providers or provided

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691 by the individuals receiving care. In survey studies, individuals that were selected for the study
692 refused to participate in the study (unit non-response) or refused to answer some questions (item
693 non-response) after agreeing to participate in the study. In each of these cases, data that are
694 determined to be useful for the assessment of the study questions are not available to the
695 investigators. As missingness has the potential to introduce bias in unpredictable ways,
696 particularly in the case where the reasons for missingness depend on the endpoint of interest,
697 FDA recommends that investigators anticipate the occurrence of missing data and establish plans
698 (in the study protocols) delineating strategies to minimize missing data, and where missingness
699 cannot be avoided, to collect or determine the reasons for the missingness, where appropriate.
700 Brick (2013), Calinescu, Schouten, and Bhulai (2012), Levy and Lemeshow (2013), and
701 Schouten, Calinescu, and Luiten (2013) discuss design strategies for improving the response rate
702 in the context of surveys. O'Neill and Temple (2012) and The National Research Council (2010)
703 discuss design strategies for the prevention of missing data in the context of clinical trials.

704 705 3. *Leveraging Existing Data*

706
707 Sometimes engaging in primary data collection methods is not practical or feasible (e.g.,
708 collecting patient experience data from ultra-rare disease populations). Therefore, FDA
709 encourages collaboration among multiple stakeholders and the use of methods to combine and
710 reuse existing data (e.g., national registry data, archival databases) to fit the specific needs of the
711 research question(s) and study goals. It is important to note that if you decide to explore the use
712 of existing data, you should demonstrate the methodological rigor of the data collection method
713 and data integrity as outlined in Section IV of this guidance.

714 715 716 **III. METHODS FOR COLLECTING AND ANALYZING PATIENT EXPERIENCE** 717 **DATA**

718
719 This section provides an overview of potential methods for collecting patient experience data and
720 considerations for analyzing patient experience data. However, FDA is open to the discussion of
721 other methods.

722
723 Three main research approaches are commonly used to help guide the collection of patient
724 experience data: qualitative research, quantitative research and mixed methods research (Johnson
725 & Christensen, 2017). Additional discussion on these methods can be found in [Appendix 1](#).

726 727 **A. Qualitative Research Methods**

728
729 ***What are qualitative research methods used for?*** Qualitative research is a method of inquiry
730 used to gain insight into the patient experience and to better understand the meaning of research
731 concepts (Johnson & Christensen, 2017; Neuman, 2014). Qualitative methods generally serve to
732 generate in-depth information about the experiences, perspectives, and feelings of patients and
733 other individuals (e.g., clinicians, caregivers), in their own words. Qualitative methods are used
734 to elicit information related to research questions, whether it is to better understand burden of
735 disease and/or treatment, or instrument design and feasibility.

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736 Qualitative research is a fluid, dynamic and evolving process. The key outcomes from this
737 method include:

738

- 739 • Understanding patient experiences, perspectives, and feelings
- 740 • Discovering and confirming research concepts (e.g., parts of the patient experience that
741 are important)
- 742 • Determining the meaning of and refining specific research concepts to measure in future
743 clinical trials
- 744 • Evaluation of respondents' understanding of COA instruments

745

746 1. *Analyzing Qualitative Data*

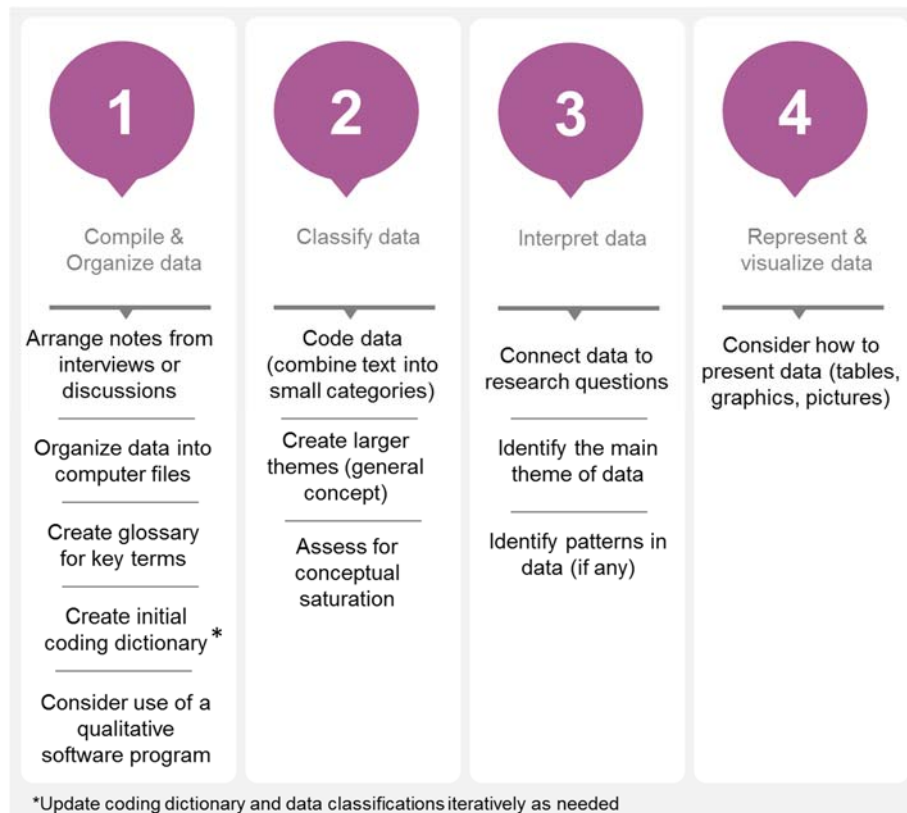
747

748 **How do you analyze data from studies using qualitative methods?** FDA recommends
749 stakeholders to consider the general steps outlined in [Figure 4](#) when analyzing qualitative data.

750

751 **Figure 4. General Steps for Data Analysis in Qualitative Research**

752



753

754 **Source:** Yin (2015), *Qualitative Research From Start to Finish* (2nd ed.), Guilford Press. Adapted with permission
755 of Guilford Press.

756

757 Qualitative research can yield quantitative data at some level (e.g., proportion of patients who
758 report a specific symptom). See [Section III.B](#) for additional details on different quantitative data
759 types. See [Section IV.A.5](#) for additional details on organizing and recording information.

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B. 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 1](#) summarizes potential aims of quantitative research.

Example: A group of psoriasis patients are administered a survey to assess the symptom burden of psoriasis (e.g., patient’s experience with psoriasis symptoms). The survey includes “closed-ended” questions with a fixed set of response options that generates a symptom score (e.g., numerical data).

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 discussion of analytical approaches to analyze quantitative data. Generally, however, the analytic approach you take depends on the following:

- research objectives. This is partly related to the aims listed in [Appendix 1 \(Table 13\)](#).
- 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 4](#) lists possible data types, descriptive approaches to summary statistics, distributional assumptions/methods for inference, and approaches to presentation of results.

Table 4. Possible approaches to quantitative data analyses and presentations

Data Types	Descriptive Statistics	Models/Methods	Data Presentation
Continuous (e.g., blood pressure level, pain score)	<ul style="list-style-type: none">• Mean/median/mode• Standard deviation• Standard error• Confidence intervals• Range	<ul style="list-style-type: none">• Normal distribution• Linear/non-linear regression• Analysis of variance• Analysis of covariance	<ul style="list-style-type: none">• Tables• Graphs (e.g., scatter/density plots)• Stratification by age groups, gender, race/ethnicity, and other subgroups of interest

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Data Types	Descriptive Statistics	Models/Methods	Data Presentation
Categorical, Count (e.g., number of hospital visits or adverse events per month; types or categories of adverse events)	<ul style="list-style-type: none"> • Frequencies • Proportions • Standard error • Confidence intervals 	<ul style="list-style-type: none"> • Binomial/Multinomial/Poisson distributions • Generalized Linear Models (Agresti, 2002; Fleiss, Levin, & Paik, 2003; McCullagh & Nelder, 1989) 	<ul style="list-style-type: none"> • Tables • Graphs • Stratification by age groups, gender, race/ethnicity, and other subgroups of interest
Longitudinal	Means, frequencies, or proportions at specific time points	See Diggle, Heagerty, Liang, and Zeger (2002) and Fitzmaurice, Laird, and Ware (2012).	<ul style="list-style-type: none"> • Tables • Graphs summarizing trend over time • Stratification by age groups, gender, race/ethnicity, and other subgroups of interest

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2. *Additional Analytical Considerations for Data Obtained Under Probability Sampling*

For data obtained under probability sampling, it is important to incorporate the design feature into the analysis by weighting each sample unit by the reciprocal of the probability of selection, as this provides a mechanism for generalizing to the target population. This weight quantity is sometimes referred to as base weights and can be interpreted as the number of individuals that each patient in the sample represents in the population.

Example: Suppose there were 100,000 individuals in the sampling frame and 2,000 were sampled, then for simple random sampling with replacement, each individual has a probability of 0.02 of being selected. In the analysis, individuals are assigned a weight of 50 as determined by the reciprocal of 0.02. That is, each patient in the sample represents 50 individuals in the target population. For multistage designs, the sampling probabilities are obtained as the product of the sampling probabilities from each stage.

In cases where the design does not make use of stratification, gains in precision may be obtained by performing a post-stratification analysis via weighting class adjustment or raking. These algorithms are discussed by Korn and Graubard (1999) and Copeland and Ganesh (2015).

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809 3. *Additional Analytical Considerations for Missing Data and Non-response*

810
811 To the extent that strategies designed to prevent or reduce missing data (see **Section II.F.2**) are
812 unsuccessful, analyses using the observed data may or may not be valid, depending on the extent
813 of missingness. FDA recommends the following:

- 814
- 815 • provide a table summary of missing data; useful information includes frequencies,
816 percentages, stratification by important subgroups, reasons for missingness.
- 817
- 818 • for longitudinal data, summarize missingness stratified by assessment visits or time
819 points.
- 820
- 821 • In addition, methods for handling missing data in analysis should be addressed in the
822 protocol. See The National Research Council (2010) and ICH E9(R1) (International
823 Council for Harmonization, 2017) for discussion of methods. Non-response missingness
824 in surveys under probability sampling could be similarly addressed by missing data
825 methods. Some of these approaches include weighting class-adjustment (Copeland &
826 Ganesh, 2015; Korn & Graubard, 1999; Valliant *et al.*, 2013), calibration adjustment
827 (Sarndal & Lundstrom, 2005), and propensity score modeling (Valliant *et al.*, 2013).

828 829 **C. Mixed Methods**

830
831 ***What is mixed methods research?*** Qualitative data and quantitative data can complement each
832 other. Mixed methods research is where both qualitative and quantitative methods are used. A
833 mixed methods study addresses a set of research questions that require both qualitative and
834 quantitative evidence and methods. Both the quantitative and qualitative data should be analyzed
835 and interpreted together before reaching a conclusion.

836
837 Mixed methods studies can occur in different ways: mixing of data, of designs, and of analyses.
838 These types of studies can be conducted within a single study or within a coordinated series of
839 studies for integrated analyses. The simplest approach to a mixed method study involves the use
840 of both qualitative and quantitative data.

841
842 A more complex approach to a mixed method study is mixing of designs. There are different
843 types of mixed designs, which may include but not limited to the following:

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Parallel (qualitative and quantitative in parallel)

- Using and analyzing open-ended (qualitative) and closed-ended (quantitative) items/questions as part of the same survey/questionnaire (Yin, 2016)
- Converting qualitative data into quantitative data through content analysis (Yin, 2016)

Sequential (qualitative first, then quantitative)

- Using qualitative data to define patient subgroups, based on observations of their experience with the disease/condition or treatment (qualitative) to identify variables or develop an instrument (Creswell & Clark, 2007; Yin, 2016)
- Using qualitative data from patients to characterize their disease experience (qualitative), and then comparing patients' responses to a survey/questionnaire (quantitative)

Sequential (quantitative first, then qualitative)

- Collecting quantitative data first and then using qualitative data to further understand the quantitative data. (Creswell & Clark, 2007; Yin, 2016).

844 Examples:

845

846 *Scenario 1:* A group of patients is administered a survey to assess the burden of Type 2 diabetes
847 (e.g., patient's experience with Type 2 diabetes, including symptoms, doctor visits, medication
848 use). The survey includes open-ended and closed-ended questions. With the use of these types
849 of questions, the survey can produce both qualitative (textual) and quantitative (numeric or
850 categorical) data.

851

852 *Scenario 2:* A *patient-reported outcome* (PRO) instrument is administered to patients in a
853 clinical trial. Exit interviews where patients are asked whether they experienced a meaningful
854 response are conducted shortly after the end of the clinical trial. Qualitative data from the
855 interviews (patients' quotes) are used in comparing the PRO results from patients who reported a
856 clinical benefit versus those who did not in order to interpret the PRO scores.

857

858 1. *Analyzing data from mixed methods*

859

860 *How do you analyze data from mixed methods?* Different types of analyses can be used to
861 analyze data from a mixed method study, including combining the use of analyses described for
862 qualitative ([Section III.A.1](#)) and quantitative ([Section III.B.1](#)) methods. FDA recommends that
863 stakeholders choose the best analysis approach for their research objective.

864

865 IV. OPERATIONALIZING AND STANDARDIZING DATA COLLECTION AND 866 DATA MANAGEMENT

867

868 A. Standard Approaches to Consider for Collecting and Managing Data

869

870 *What activities occur during data collection?* There are a series of inter-related activities in the
871 process of collecting data, which include the following (Creswell, 2013):

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- Locating patients/sites
- Gaining access
- Sampling strategy
- Collecting data
- Recording information
- Resolving site/field issues
- Managing and storing data

873
874 FDA encourages stakeholders to carefully plan these activities. Further, FDA recommends that
875 stakeholders standardize data collection activities and methods to manage data quality to the
876 extent possible.

877 1. *Locating Patients/Sites*

878
879 A critical step in the process of data collection is to identify the appropriate sample and/or sites
880 to study. In order to have adequate generalization for multicenter clinical trials, patients should
881 generally not be located from a single site. FDA generally recommends including patients from
882 diverse sites to provide a complete picture of the topic of interest (see [Section II.D.2](#) on
883 representativeness).

884 2. *Human Subjects Protection*

885
886 Research involving access to patient information or involves directly engaging with patients
887 requires careful consideration of Federal, State, and local laws and institutional policies for the
888 protection of human subjects. Because this guidance focuses on sampling methods for collecting
889 patient experience data through a variety of research contexts (including, but limited to, clinical
890 trials, observational studies, advisory boards, public meetings, etc.), a full discussion of which
891 laws may apply to these collection methods is beyond the scope of this guidance. Research
892 subject to FDA regulations must satisfy the requirements for informed consent at 21 CFR part 50
893 and the IRB requirements at 21 CFR part 56.^{14,15} Research supported or conducted by the
894 Department of Health and Human Services must satisfy the requirements at 45 CFR part 46.¹⁶
895 FDA recommends that researchers work with their Institutional Review Boards (IRBs) and
896 Health Insurance Portability and Accountability Act (HIPAA) Privacy Boards to determine what
897 laws may apply.

898
899 FDA recommends research involving patient information be conducted in accordance with the
900 principles of good clinical practice (GCP), including the International Conference on
901 Harmonisation Guidelines (see [Appendix 2](#)).

904

¹⁴ Details on 21 CFR part 50 can be found at <https://www.ecfr.gov/cgi-bin/text-idx?SID=7d2cb8de0c8bebe70c93835ce013cdd3&mc=true&node=pt21.1.50&rgn=div5>

¹⁵ Details on 21 CFR part 56 can be found at <https://www.ecfr.gov/cgi-bin/text-idx?SID=7d2cb8de0c8bebe70c93835ce013cdd3&mc=true&node=pt21.1.56&rgn=div5>

¹⁶ Details on 45 CFR part 46 can be found at <https://www.ecfr.gov/cgi-bin/text-idx?SID=991d81fee482f9aa6ef549a0067a86e8&mc=true&node=pt45.1.46&rgn=div5>

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905 3. Sampling Strategy

906
907 Of similar importance within the data collection process is the determination of a strategy for the
908 sampling of patients or sites. Refer to [Section II.D.1](#) on the different types of sampling.
909

910 4. Collecting Data

911 Stakeholders should consider which data collection approach is most appropriate for their
912 research objective. Data collection methods can include but are not limited to the following:
913

- 914 • Observations
- 915 • Interviews
- 916 • Documents (including questionnaires)
- 917 • Audiovisual materials
- 918 • Digital Health Technology

919
920 Each of the four data collection methods generates different types of data (see [Table 5](#)), each of
921 which has its own advantages and limitations. Some examples of data types are listed in [Table 5](#).
922 Additional detail, including potential advantages and limitations of each method, are discussed in
923 subsections following the table.
924

925
926 **Table 5. Data Collection Methods and Types of Data for Qualitative and Quantitative**
927 **Research**
928

Data Collection Method	Illustrative types of data	Specific examples of data
<i>Interviews and Focus Groups</i>	Language (verbal and body)	A person's description/explanation of some behavior or action; a memory; a belief or viewpoint (e.g., email, face-to-face, focus group, online focus group, telephone interviews; Delphi panel)
<i>Observations</i>	People's gestures; social interactions; actions; scenes and the physical environment	The communication/dynamics between two or more individuals; spatial arrangements of a person and a setting; efficiency of an intervention (e.g., time and motion studies)
<i>Documents</i>	Contents of: personal documents, other printed materials (e.g., literature), graphics, archival records, and physical artifacts	Information from public documents (e.g., official memos, minutes, records, archival material); medical records, chart audits; photo elicitation (participants take photographs or videotapes); scientific publications
<i>Questionnaires</i>	Set of questions (items) with a choice of answers (responses)	A person's response to a set of questions (e.g., surveys; clinical outcome assessments, such as patient-reported outcome instruments, observer-reported outcome instruments, clinician-reported outcome instruments)

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Data Collection Method	Illustrative types of data	Specific examples of data
<i>Audiovisual Materials</i>	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 with audiovisual attachments; video chat/conferencing (e.g., Skype)
<i>Social Media and Identifiable Patient Communities</i>	Contents of: conversations or text (including elicited and non-elicited content) from online communities & social media interactions, online focus groups and interviews	Information on a disease or condition (e.g., symptoms and impacts) or individual patient experiences with a disease or condition as reported by patients in online patient groups (e.g., blogs, forums, message boards) and social media pages; phone (SMS/text messages), live video/chat conferencing or messaging
<i>Digital Health Technology</i>	Mobile health, health information technology, wearable devices, telehealth and telemedicine, and personalized medicine	Information from mobile health technology (e.g., accelerometers, heartrate trackers, etc.); information from certain mobile applications

929 **Source:** Adapted from Yin (2015), *Qualitative Research From Start to Finish* (2nd ed.), Guilford Press. Adapted
 930 with permission of Guilford Press.
 931

a. Interviews and Focus Groups

934 Different interview types are used to collect patient experience data, including one-on-one
 935 interviews (semi-structured, structured or open-ended or group interviews (focus groups). The
 936 method of interviewing (e.g., in person, telephone or by video chat) may vary depending on the
 937 goals of the interview. For example, if visual cues are important for the context of the research
 938 objective, an appropriate data collection method may be face-to-face interviews either in-person
 939 or by video chat instead of telephone interviews. Further details and considerations regarding the
 940 different interview methods will be found in future guidances.

b. Observations

944 Observation can be a tool to collect patient experience data, and can include but is not limited to
 945 the observation of the interactions of a participant in particular setting, activity, or behavior
 946 (Creswell, 2013). Observations are helpful in situations for individuals who have barriers to
 947 communicating their thoughts orally or in writing. Additionally, observations of individuals or
 948 groups often can be done to supplement interviews (individual or group) by documenting cues
 949 from the environment and behaviors such as facial expressions, gestures, tone of voice, and other
 950 non-verbal indicators.

c. Documents

953 Various types of documents can be used to collect patient and/or caregiver input on burden of
 954 disease and treatment, some of which are listed in [Table 5](#).

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956 d. Questionnaires

957
958 Surveys or questionnaires can be used in observational studies to capture patient experience data.
959 Questionnaires can also be used to collect patient-reported outcomes in clinical trials. This is a
960 specific use to evaluate a patient’s response to treatment and it necessitates certain measurement
961 properties that will be described in detail in later guidances.

962
963 ***What are questionnaires?*** Questionnaires generally consist of a standard set of questions or
964 items that are generally administered in the same order to each participant, but can be
965 administered via computerized adaptive testing (Johnson & Christensen, 2017). Questionnaires
966 can be administered in both observational studies and clinical trials. In these settings, data can be
967 collected by questionnaires throughout the study or at the end of the study (e.g., exit surveys).

968
969 Exit surveys are a standardized method used to collect information about various experiences,
970 including treatment satisfaction and study experience with minimal recall bias (Geldsetzer, Fink,
971 Vaikath, & Barnighausen, 2018). Exit surveys are generally administered at the end of a
972 participants’ enrollment in a study. However, surveys also can be administered at multiple time
973 points throughout the study (Hrisos *et al.*, 2009; Turner, Angeles, Tsui, Wilkinson, & Magnani,
974 2001).

975
976 Questionnaires can be administered in different modes:

- 977
- 978 • In-person paper administration: paper questionnaires filled out in person by the
979 participant
 - 980
 - 981 • Interviewer administration: questionnaire administered by an interviewer following a
982 structured protocol
 - 983
 - 984 • Telephone questionnaire administration: questions administered over the phone
985
 - 986 • Electronic administration: participants can complete questions via email, web interface,
987 or electronic device
 - 988
 - 989 • Interactive voice response systems: questions administered over an automated telephone
990 system

991
992 ***What are some key considerations when using questionnaires to collect patient experience***
993 ***data?*** When using questionnaires to collect patient experience data, FDA generally recommends
994 the following:

- 995
- 996 • Each participant in a sample is asked the same set of questions to the extent possible
 - 997 • Design questions that are interpreted and understood well by participants
 - 998 • Pre-test/pilot-test questions
 - 999 • Avoid using incomplete questions (e.g., Age? Reason last saw doctor?)

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- 1000 • Avoid using questions that ask two or more concepts at once (e.g., How embarrassed or
1001 self-conscious have you been because of your condition?)
1002 • Create distinct and non-overlapping response options for each question
1003

1004 If questionnaires are intended to be used in observational survey studies (paper or electronic-
1005 based), FDA encourages the following steps (Cooper *et al.*, 2006):
1006

- 1007 • Select pool of participants or panelists (e.g., health panels) to be observed. Obtain the
1008 required permissions needed to gain access to the participants and/or panelists.
1009 • Create a system in which questions can be entered, as well as possible responses, into a
1010 database table.
1011 • Generate tables to record the data entered through the questionnaire from the database
1012 table of questions and possible responses.
1013 • Develop a simple, user-friendly paper-based or electronic-based questionnaire.
1014 • Provide data validation during the entry process.
1015 • Develop a coding manual that could be used as a reference document.
1016 • For web-based surveys, generate descriptive statistics that could be observed through the
1017 web during the entry phase of the questionnaire.
1018 • Develop program files that allow opportunity to do more advanced statistics once the
1019 questionnaire is completed.
1020 • Maintain a database to access the questionnaire table and data entered into the
1021 questionnaire. This database should have built-in features or capacity to interface with
1022 software that has features such as forms, queries, and reports to further work with the
1023 data.
1024

1025 If questionnaires are intended to be a study endpoint in a clinical trial, FDA recommends that
1026 stakeholders adopt good measurement principles. Refer to the FDA PRO Guidance (FDA, 2009)
1027 on factors to consider when administering questionnaires in clinical trials. Refer to [Appendix 2](#)
1028 regarding standards and requirements pertaining data submission to FDA.
1029

e. Audiovisual Materials

1030 Audiovisual materials (e.g., audiotape, videotape, photographs, social media) also can be used to
1031 collect data in characterizing the patient experience (see [Table 5](#)).
1032

1033 Steps to consider when using audiovisual materials in the data collection process include:
1034

- 1035 • Obtain the required permissions needed to use materials, including informed consent.
1036 • Obtain permission to extract information from web content, if necessary (e.g., request
1037 permission to join online forums and inquire whether there are restrictions on use of
1038 information for research purposes).
1039

f. Social Media and Identifiable Patient Communities

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1044 FDA encourages external stakeholders to explore the use of **social media** tools (e.g., medical
 1045 community blogs; crowdsourcing; and social media pages) to shed light on patients’ perspectives
 1046 regarding symptoms and impacts of a disease or condition. Targeted social media searches may
 1047 be useful during the preliminary stages of a study to complement literature review findings,
 1048 inform the development of research tools (e.g., qualitative study discussion guides) or as a
 1049 supplement to traditional research approaches (e.g., literature, one-on-one interviews, focus
 1050 groups or expert opinion).

1051
 1052 Common methods for generating patient input through social media, along with some potential
 1053 strengths and limitations of these methods, are detailed in [Table 6](#).

1054
 1055 **Table 6. Common Methods for Gathering Patient Input Using Social Media**
 1056

Social Media Qualitative Research Methodology	Strengths	Limitations
<i>All social methodologies</i>	<ul style="list-style-type: none"> • May allow access to hard to reach populations • Cost & time saving for researchers • Relatively easy to implement • Accurate & automatic capture of data • Participant convenience & comfort • Greater self-disclosure 	<ul style="list-style-type: none"> • Self-selection bias (social media participants may include a narrow band of patients with regard to clinical or demographic characteristics)
<p><i>Asynchronous online focus groups or interviews (occur at different places, different times)</i></p> <p>(Tates <i>et al.</i>, 2009; Wilkerson, Iantaffi, Grey, Bockting, & Rosser, 2014)</p>	<ul style="list-style-type: none"> • Can be conducted using email, discussion forums, and other forms of social media • Provide flexibility and convenience of logging in at own place and time • Lack of time pressure & greater reflection 	<ul style="list-style-type: none"> • Lack of visual cues • Underlying selection process might be difficult, if not impossible, to quantify • Representativeness might be questionable without strong assumptions
<p><i>Synchronous online focus groups or interviews (among younger participants; occur at different places, same time [for focus groups])</i></p> <p>(Fox, Morris, & Rumsey, 2007; Wilkerson <i>et al.</i>, 2014)</p>	<ul style="list-style-type: none"> • Data captured in real-time (synchronous) • Can be conducted using the phone (SMS/text messages), chat methods, video messaging • Interaction is often dynamic, immediate, conversational (similar to everyday interactions) • Assessment of visual cues (through video or emotions) 	<ul style="list-style-type: none"> • Scheduling can be difficult; must find a common meeting time (for focus groups) • Requires a fast internet connection, webcam/ audio/video capabilities which some participants may not have readily available • Technology rich interface can present more technical difficulties

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Social Media Qualitative Research Methodology	Strengths	Limitations
	<p>conveyed through emoticon use)</p> <ul style="list-style-type: none"> • Less threatening methodology for younger participants 	<ul style="list-style-type: none"> • Moderation can be difficult with too many participants; sometimes participants have trouble taking turns (for focus groups) • Faster typing speed gives participants an advantage and these participants can dominate the conversation (for focus groups) • Increased likelihood of passive participation (e.g., a participant logging on and observing but not participating) • Groups with more than 5 participants require 2 moderators (for focus groups) • Self-selection bias (social media participants may include a narrow band of patients with regard to clinical or demographic characteristics)
<p style="text-align: center;"><i>Designed online communities and social media data collection</i></p> <p>(Grajales <i>et al.</i>, 2014; Paulus & Lester, 2013; Varga & Paulus, 2014)</p>	<ul style="list-style-type: none"> • Generated through platforms like online support groups and online educational groups • Groups include identifiable patients and identifiable reporters • Helpful for: <ul style="list-style-type: none"> - gathering information on health conditions (Prieto <i>et al.</i>, 2014) - sharing treatments and experiences of care (McGregor <i>et al.</i>, 2014) - recruiting research participants (O'Connor, Jackson, Goldsmith, & Skirton, 2014) 	<ul style="list-style-type: none"> • Must have authorization to obtain identifiable information (e.g., Personal Health Information (PHI))
<p style="text-align: center;"><i>Spontaneous online communities and social</i></p>	<ul style="list-style-type: none"> • Generated through easily accessible platforms 	<ul style="list-style-type: none"> • Participants are unknown; Respondent identification not verifiable

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Social Media Qualitative Research Methodology	Strengths	Limitations
<i>media data collection (unelicited data)</i> (Grajales, Sheps, Ho, Novak-Lauscher, & Eysenbach, 2014)	<ul style="list-style-type: none">• Low burden for people providing data• Helpful for:<ul style="list-style-type: none">- gathering information on health conditions (Prieto, Matos, Alvarez, Cacheda, & Oliveira, 2014)	<ul style="list-style-type: none">• PHI not verifiable• Underlying selection process is difficult if not impossible to quantify• Representativeness is highly questionable without strong assumptions

1057
1058 While social media tools can provide useful data, limitations related to sampling need to be
1059 considered. With most social media sources, there is no mechanism for verifying patient identity,
1060 or clinical and demographic characteristics; you must rely on patient self-identification and
1061 diagnosis, which can be inaccurate. Additionally, different demographic groups tend to use
1062 different types of social media (e.g., Pinterest is often dominated by female users, Instagram is
1063 dominated by young adults). Based on this variability, you may need to use different social
1064 media tools to gather information from the demographic group(s) you are targeting. Likewise,
1065 when submitting information for regulatory review, you would have to demonstrate how the data
1066 collection methods used to generate data addresses these limitations and to ensure rigor in
1067 methodology and data integrity.

1068
1069 It may be possible to mitigate concerns around the lack of ability to confirm patient
1070 characteristics (e.g. diagnosis) in various ways. For example, to have an identifiable patient,
1071 there should be enough information to indicate the existence of a specific patient, including but
1072 not limited to age (or age category, e.g., adolescent, adult, elderly), gender, initials, date of birth,
1073 name, or patient identification number. Clinical information may also be available, by
1074 permission, through a central database (e.g., for patients who are members of patient advocacy
1075 group message boards, social networking groups, or medical community blogs). An identifiable
1076 reporter can be a family member, doctor, other health care practitioner, or other individual who
1077 has sufficient information to indicate that they are an identifiable person who has knowledge
1078 about the patient.

1079 g. Digital Health Technology

1080
1081
1082 Digital health technology can be one approach to mobile data collection and can include devices
1083 that allow participants to track some aspect of their health data. FDA recommends stakeholders
1084 who are collecting patient experience data with digital health technology to discuss the planned
1085 method early with FDA and obtain feedback from the relevant FDA review division.

1086 5. Recording Information

1087
1088
1089 FDA recommends that stakeholders develop written forms or protocols to collect patient
1090 experience data, such as a discussion guide or observational protocol. A discussion guide or
1091 observational protocol is a pre-designed form used to record information collected during an
1092 interview or observation (e.g., interviewer may take notes on the discussion guide or

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1093 observational protocol). Patient experience data can also be recorded through various forms, such
1094 as interview summaries and audio-and video-recordings.

1095

1096 6. *Resolving Site/Field Issues*

1097

1098 FDA recommends that standardized training be provided to the members of the research team to
1099 improve consistency of research. The roles and responsibilities of the team should be outlined in
1100 the research protocol. This will help to prevent many site issues. FDA encourages stakeholders
1101 to also have a troubleshooting guide. Researcher(s) should anticipate and address site/field issues
1102 that might arise during data collection. Some issues to consider are listed below (Creswell, 2013):
1103

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., administering correct version of the questionnaire, looking for non-response patterns, such as not completing a particular section)

Electronic 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, Audiovisual materials, Digital Health Technology

- Locating materials
- Obtaining permission from the participant to use materials (e.g., audio-/video-recorder)
- Minimal noise disturbance
- Best location for video recorder/camera

Ethical issues

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- Informed consent, if required
- IRB oversight, if required
- Conflicts of interest
- Dishonest or hidden (secret) activities
- Confidentiality and privacy considerations
- Benefits of research to participants, and risks

1104 7. *Data Management*

1105
1106 FDA recommends that data management be addressed in the early stages of a research study.
1107 Before initiating data collection, you should formulate a data management plan (DMP)—a
1108 written document that describes the data you expect to acquire or generate during your research
1109 study; how you intend to manage, describe, analyze, and store said data; and what mechanisms
1110 you will use at the end of your study to preserve and share your data (Stanford University
1111 Libraries, n.d.-a); creating a written DMP helps formalize the data management process, identify
1112 potential weaknesses in the DMP, and provides a record of what you intend(ed) to do. See
1113 [Appendix 3](#) for resources to consider when developing a data management plan, as well as
1114 components of a good data management plan.

1115 8. *Data Standards*

1116
1117 External stakeholders should use appropriate data standards when collecting, managing, and
1118 reporting patient experience data. When planning a study (including the design of case report
1119 forms, data management systems, and statistical analysis plans), you should determine which
1120 FDA-supported standards to use or request a waiver of those requirements. There may be
1121 versions of a standard available that are not yet supported by FDA (e.g., specific SDTM or
1122 ADaM versions) or there may be FDA-supported standards that, currently, have only specific
1123 components developed (e.g., SEND study types).¹⁷ See [Appendix 2](#) for some data standards
1124 resources.

1125
1126 While compliance with these standards may not be required for studies¹⁸ other than those
1127 conducted to support a regulatory medical product application (e.g., an IND, NDA, or BLA) or
1128 medical product labeling language, we encourage researchers to, at a minimum, bear these
1129 standards in mind, because patient experience data that are ultimately intended for use in clinical
1130 studies *would* be subject to the applicable standards.

1131 9. *Monitoring and Quality Assurance*

1132
1133 FDA expects that external stakeholders will be responsible for monitoring the study, ensuring
1134 data integrity, and performing the data analysis.

1135
1136

¹⁷ Study Data Tabulation Model (SDTM), Analysis Data Model (ADaM), Standard for Exchange of Nonclinical Data (SEND), available at www.cdisc.org.

¹⁸ Such as stand-alone psychometric validation studies submitted to the COA Drug Development Tool (DDT) Qualification Program

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1137 10. *Storing Data*

1138
1139 FDA recommends that external stakeholders plan how to store their data in advance of starting
1140 their study. Researchers should decide how data will be best stored so that it can be easily
1141 retrieved and protected from any type of damage or loss. The approach to data storage should
1142 reflect the type of data collected. Regarding the length of time to keep records of data,
1143 researchers should comply with their IRB and applicable regulations.

1144
1145 Principles to consider about data storage and handling data include the following (Creswell,
1146 2013):

- 1147
- 1148 • Create back-up copies of computer files
- 1149 • Use high-quality equipment for audio-recording information during interviews
- 1150 • Protect the anonymity of participants by de-identification
- 1151 • Create a data collection table or database to track and identify data
- 1152 • Maintain a list of types of data collected

1153 11. *Confidentiality*

1154
1155
1156 All personal participant data collected and processed for research should be managed by the
1157 research team with adequate precautions to ensure confidentiality of the data in accordance with
1158 applicable national and/or local laws and regulations on personal data protection.

1159 **V. CONCLUSIONS**

1160
1161
1162 This document has provided an overview of methods to collect robust, meaningful, and
1163 sufficiently representative patient input to inform medical product development and regulatory
1164 decision making. The proposed methods presented serve only as a basis for dialogue in the
1165 evolving and growing area of the science of patient input. If you are considering collecting
1166 patient experience data, FDA encourages you to have early interactions with FDA and obtain
1167 feedback from the relevant FDA review division on appropriate research design and any
1168 applicable regulatory requirements.

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1330 GLOSSARY

1331

1332 This glossary defines terms that will be used in the series of methodological Patient-Focused
1333 Drug Development (PFDD) FDA guidance documents that are required by the 21st Century
1334 Cures Act, and part of commitments made by FDA under the sixth authorization of the
1335 Prescription Drug User Fee Act (PDUFA VI). The goal of this glossary is to provide
1336 standardized nomenclature and terminologies related to patient-focused medical product
1337 development. As appropriate, definitions from existing federal resources (e.g., BEST
1338 (Biomarkers, Endpoints, and Other Tools) Resource) have been incorporated into this glossary.
1339 External resources were also utilized to define terms and have been cited.

1340

1341 **Attribute:** An attribute is a feature or characteristic of a medical product—such as efficacy or
1342 effectiveness, safety, means of administration, duration of effect, or duration of use—that may
1343 affect benefit-risk considerations.

1344

1345 **Benefit:** Benefits are the favorable effects of a medical product. Types of benefit include clinical
1346 benefit (*see definition below*). Benefits may also include important characteristics of the medical
1347 product, such as convenience (e.g., a more convenient dosing regimen or route of administration)
1348 that may lead to improved patient compliance, or benefits that affect those other than the patient.
1349 (*Source: [International Conference on Harmonisation \(ICH\) Guidelines – Efficacy M4E\(R2\)](#)*)

1350

1351 **Benefit-risk assessment:** Evaluation of the demonstrated benefits and risks of a medical product
1352 and making a judgment as to whether the expected benefits outweigh the potential risks
1353 associated with its expected use.

1354

1355 **Biomarker:** A defined characteristic that is measured as an indicator of normal biological
1356 processes, pathogenic processes, or responses to an exposure or intervention, including
1357 therapeutic interventions. Molecular, histologic, radiographic, or physiologic characteristics are
1358 types of biomarkers. A biomarker is not an assessment of how an individual feels, functions, or
1359 survives. (*Source: [BEST \(Biomarkers, Endpoints and Other Tools\) Resource](#)*)

1360

1361 **Caregiver:** A person who helps a patient with daily activities, health care, or any other activities
1362 that the patient is unable to perform himself/herself due to illness or disability, and who
1363 understands the patient's health-related needs. This person may or may not have decision-
1364 making authority for the patient and is not the patient's healthcare provider.

1365

1366 **Caregiver preference:** A statement of the relative desirability or acceptability to caregivers of
1367 attributes by which alternative health interventions may differ.

1368

1369 **Clinical benefit:** A positive clinically meaningful effect of an intervention, e.g., a positive effect
1370 on how an individual feels, functions, or survives. (*Source: [BEST \(Biomarkers, Endpoints and
1371 Other Tools\) Resource](#)*)

1372

1373 **Clinical outcome:** An outcome that describes or reflects how an individual feels, functions or
1374 survives. (*Source: [BEST \(Biomarkers, Endpoints and Other Tools\) Resource](#)*)

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1375
1376 **Clinical outcome assessment:** Assessment of a clinical outcome can be made through report by
1377 a clinician, a patient, a non-clinician observer or through a performance-based assessment. There
1378 are four types of COAs: patient-reported outcome (PRO), clinician-reported outcome (ClinRO)
1379 measures, observer-reported outcome (ObsRO), and performance outcome (PerfO). (Source:
1380 [BEST \(Biomarkers, Endpoints and Other Tools\) Resource](#))

1381
1382 **Clinical relevance:** The extent to which an endpoint can capture and measure an aspect of a
1383 potential clinical benefit (improvement in how the patient feels, functions, and/or survives) that
1384 is important from a clinical perspective and from the patient's perspective.

1385
1386 **Clinician-reported outcome (ClinRO):** A measurement based on a report that comes from a
1387 trained health-care professional after observation of a patient's health condition. Most ClinRO
1388 measures involve a clinical judgment or interpretation of the observable signs, behaviors, or
1389 other manifestations related to a disease or condition. ClinRO measures cannot directly assess
1390 symptoms that are known only to the patient (e.g., pain intensity). (Source: [BEST \(Biomarkers,](#)
1391 [Endpoints and Other Tools\) Resource](#))

1392
1393 **Concept (also referred to as concept of interest):** In a regulatory context, the concept is the
1394 aspect of an individual's clinical, biological, physical, or functional state, or experience that the
1395 assessment is intended to capture (or reflect). (Source: [BEST \(Biomarkers, Endpoints and Other](#)
1396 [Tools\) Resource](#))

1397
1398 **Data analysis plan:** A roadmap for how the data will be organized and analyzed and how results
1399 will be presented. A data analysis plan should be established when planning a research study
1400 (i.e., before data collection begins). Among other things, the data analysis plan should describe:
1401 (a) the data to be collected; (b) the analyses to be conducted to address the research objectives,
1402 including assumptions required by said analyses; (c) data cleaning and management procedures;
1403 (d) data transformations, if applicable; and (e) how the study results will be presented (e.g.,
1404 graphs, tables).

1405
1406 **Data management plan (DMP):** A written document that describes the data you expect to
1407 acquire or generate during the course of your research study; how you intend to manage,
1408 describe, analyze, and store said data; and what mechanisms you will use at the end of your
1409 study to preserve and share your data. (Source: [Stanford University Libraries n.d.\(b\)](#))

1410
1411 **Disease burden:** The impacts, direct and indirect, of the patient's health condition that has a
1412 negative effect on his or her health, functioning, and overall well-being. Disease burden includes
1413 (but is not limited to): the physical and physiologic impacts of the disease and its symptoms; co-
1414 morbidities; emotional and psychological effects of the disease, its management, or prognosis;
1415 social impacts; effects on relationships; impacts on the patient's ability to care for self and
1416 others; time and financial impacts of the disease and its management; and considerations on the
1417 impacts on the patient's family.

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1419 **Endpoint:** A precisely defined variable intended to reflect an outcome of interest that is
1420 statistically analyzed to address a particular research question. A precise definition of an
1421 endpoint typically specifies the type of assessments made, the timing of those assessments, the
1422 assessment tools used, and possibly other details, as applicable, such as how multiple
1423 assessments within an individual are to be combined. (Source: [BEST \(Biomarkers, Endpoints
1424 and Other Tools\) Resource](#))

1425
1426 **Fit-for-purpose:** A conclusion that the level of validation associated with a medical product
1427 development tool is sufficient to support its context of use. (Source: [BEST \(Biomarkers,
1428 Endpoints and Other Tools\) Resource](#))

1429
1430 **Generalizability:** The extent to which study findings can be reliably extended to the target
1431 population of interest.

1432
1433 **Health literacy:** The degree to which individuals have the capacity to obtain, process, and
1434 understand basic health information and services needed to make appropriate health decisions.
1435 (Source: U.S. Department of Health and Human Services [Quick Guide to Health Literacy](#))
1436 Health literacy also includes numeracy skills—such as calculating cholesterol and blood sugar
1437 levels, measuring medication doses, and understanding nutrition labels—and knowledge of
1438 health topics.

1439
1440 **Literacy:** A person's ability to read, write, speak, and compute and solve problems at levels
1441 necessary to: (a) function on the job and in society; (b) achieve one's goals; and (c) develop one's
1442 knowledge and potential. (Source: U.S. Department of Health and Human Services [Quick Guide
1443 to Health Literacy](#))

1444
1445 **Methodologically sound:** Assurance that the methods and processes used to obtain and analyze
1446 patient experience data are rigorous, robust, and adhere to scientifically established principles
1447 and best practices for method development or implementation. Evidence generated by
1448 methodologically sound methods and processes increases confidence that the results can be
1449 trusted, interpreted, and support the intended regulatory uses.

1450
1451 **Mixed methods research:** Research that uses both qualitative and quantitative research
1452 methods. See definitions for qualitative and quantitative research methods.

1453
1454 **Observer-reported outcome (ObsRO):** A measurement based on a report of observable signs,
1455 events or behaviors related to a patient's health condition by someone other than that patient or a
1456 health professional. Generally, ObsROs are reported by a parent, caregiver, or someone who
1457 observes the patient in daily life and are particularly useful for patients who cannot report for
1458 themselves (e.g., infants or individuals who are cognitively impaired). An ObsRO measure does
1459 not include medical judgement or interpretation. (Source: [BEST \(Biomarkers, Endpoints and
1460 Other Tools\) Resource](#)). Examples of ObsROs include a parent report of a child's vomiting
1461 episodes or a report of wincing thought to be the result of pain in patients who are unable to
1462 report for themselves.

1463

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1464 **Patient:** Any individual with or at risk of a specific health condition, whether or not he or she
1465 currently receives any therapy to prevent or treat that condition. Patients are the individuals who
1466 directly experience the benefits and harms associated with medical products.

1467

1468 **Patient advocate:** An individual or group of individuals, who may or may not be part of the
1469 target patient population, who has a role in promoting an interest or cause to influence policy
1470 with respect to patients' health or healthcare.

1471

1472 **Patient-centered:** See *patient-focused*

1473

1474 **Patient-centered outcome:** An outcome that is important to patients' survival, functioning, or
1475 feelings as identified or affirmed by patients themselves, or judged to be in patients' best interest
1476 by providers and/or caregivers when patients cannot report for themselves. (Source: *ISPOR*
1477 *Plenary*, [Patrick 2013](#))

1478

1479 **Patient engagement:** Activities that involve patient stakeholders sharing their experiences,
1480 perspectives, needs, and priorities that help inform FDA's public health mission. Such activities
1481 may include (but are not limited to): testimony at Advisory Committee meetings, submission to
1482 regulations.gov public docket; meetings attended by patients, FDA, and other stakeholders; other
1483 correspondence with FDA; interactions through social media; and interactions with or
1484 information from patient representatives or patient advocates.

1485

1486 **Patient experience data:** Defined in Title III, section 3001 of the 21st Century Cures Act, as
1487 amended by section 605 of the FDA Reauthorization Act of 2017 (FDARA),¹⁹ and includes data
1488 that are collected by any persons and are intended to provide information about patients'
1489 experiences with a disease or condition. Patient experience data can be interpreted as information
1490 that captures patients' experiences, perspectives, needs, and priorities related to (but not limited
1491 to): 1) the symptoms of their condition and its natural history; 2) the impact of the conditions on
1492 their functioning and quality of life; 3) their experience with treatments; 4) input on which
1493 outcomes are important to them; 5) patient preferences for outcomes and treatments; and 6) the
1494 relative importance of any issue as defined by patients.

1495

1496 **Patient-focused** (also referred to as *patient-centered*): Ensuring that patients' experiences,
1497 perspectives, needs, and priorities are meaningfully incorporated into decisions and activities
1498 related to their health and well-being.

1499

1500 **Patient-focused drug development (PFDD)** (also referred to as *patient-focused medical*
1501 *product development*): A systematic approach to help ensure that patients' experiences,

¹⁹ "PATIENT EXPERIENCE DATA.—For purposes of this section, the term 'patient experience data' includes data that (1) are collected by any persons (including patients, family members and caregivers of patients, patient advocacy organizations, disease research foundations, researchers, and drug manufacturers); and (2) are intended to provide information about patients' experiences with a disease or condition, including (A) the impact (including physical and psychosocial impacts) of such disease or condition, or a related therapy, on patients' lives; and (B) patient preferences with respect to treatment of such disease or condition." The definition is codified at section 569C(c)(4) of the FD&C Act, and applies to section 3002 of the 21st Century Cures Act, which directed FDA to issue certain guidance documents regarding the collection of patient experience data, see section 3002(b).

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1502 perspectives, needs, and priorities are captured and meaningfully incorporated into the
1503 development and evaluation of medical products throughout the medical product life cycle.

1504
1505 **Patient input:** Information that captures patients' experiences, perspectives, needs, and
1506 priorities. See *Patient Experience Data*.

1507
1508 **Patient partner:** An individual patient, caregiver or patient advocacy group that engages other
1509 stakeholders to ensure the patients' wants, needs and preferences are represented in activities
1510 related to medical product development and evaluation. (Source: Wilson *et al*, 2018)

1511
1512 **Patient perspective:** A type of patient experience data that specifically relates to patients'
1513 attitudes or points of view about their condition or its management. Patient perspectives may
1514 include (but are not limited to): perceptions, goals, priorities, concerns, opinions, and
1515 preferences.

1516
1517 **Patient preference:** A statement of the relative desirability or acceptability to patients of
1518 specified alternatives or choice among outcomes or other attributes that differ among alternative
1519 health interventions. (Source: [FDA Guidance on PPI for medical devices](#))

1520
1521 **Patient preference information (PPI):** Assessments of the relative desirability or acceptability
1522 to patients of specified alternatives or choices among outcomes or other attributes that differ
1523 among alternative health interventions. The methods for generating PPI may be qualitative,
1524 quantitative, or mixed methods. (Source: [FDA Guidance on PPI for medical devices](#))

1525
1526 **Patient-provided input:** *Patient experience data* or other information that comes directly from
1527 patients.

1528
1529 **Patient-reported outcome (PRO):** A measurement based on a report that comes directly from
1530 the patient (i.e., study subject) about the status of a patient's health condition without
1531 interpretation of the patient's response by a clinician or anyone else. A PRO can be measured by
1532 self-report or by interview, provided that the interviewer records only the patient's response.
1533 Symptoms or other unobservable concepts known only to the patient (e.g., pain severity or
1534 nausea) can only be measured by PRO measures. PROs can also assess the patient perspective
1535 on functioning or activities that may also be observable by others. (Source: [BEST \(Biomarkers,
1536 Endpoints and Other Tools\) Resource](#))

1537
1538 **Patient representative:** An individual, who may or may not be part of the target population,
1539 who has direct experience with a disease or condition (e.g., a patient or caregiver) and can
1540 provide information about a patient's experience with the disease or condition.

1541
1542 **Performance outcome (PerfO):** A measurement based on a standardized task(s) performed by a
1543 patient that is administered and evaluated by an appropriately trained individual or is
1544 independently completed. PerfOs require patient cooperation and motivation. These include
1545 measures of gait speed (e.g., timed 25 foot walk test), memory recall (e.g., word recall test), or

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1546 other cognitive testing (e.g., digit symbol substitution test). (Source: [BEST \(Biomarkers,](#)
1547 [Endpoints and Other Tools\) Resource](#))

1548
1549 **Qualitative research methods:** Methods associated with the gathering, analysis, interpretation,
1550 and presentation of narrative information (e.g., spoken or written accounts of experiences,
1551 observations, and events). Qualitative research methods may also include direct observations
1552 (e.g., non-verbal communication and behaviors).

1553
1554 **Quantitative research methods:** Methods associated with the gathering, analysis,
1555 interpretation, and presentation of numerical information.

1556
1557 **Real-World Data (RWD):** Data relating to patient health status and/or the delivery of health
1558 care routinely collected from a variety of sources. (Source: [FDA Guidance on Use of Real-World](#)
1559 [Evidence to Support Regulatory Decision-Making for Medical Devices](#))

1560
1561 **Real world evidence (RWE):** The clinical evidence regarding the usage and potential benefits
1562 or risks of a medical product derived from analysis of real-world data. (Source: [FDA Guidance](#)
1563 [on Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices](#))

1564
1565 **Reporter:** In research studies designed to collect patient experience data, the reporter is the
1566 individual, group of individuals, or entity providing patient experience data. Reporters may be
1567 patients, parents, sexual/romantic partners, caregivers, physicians, or other healthcare
1568 professionals. Selection of an appropriate reporter in a given research study will depend on the
1569 definition of the target patient population of interest. If a patient in the target population can be
1570 reasonably expected to reliably self-report, then one would expect the patient herself/himself to
1571 be the reporter in that research study.

1572
1573 **Representativeness:** Confidence that a sample from which evidence is generated is sufficiently
1574 similar to the intended population. In the context of patient experience data, representativeness
1575 includes the extent to which the elicited experiences, perspectives, needs, and priorities of the
1576 sample are sufficiently similar to those of the intended patient population.

1577
1578 **Research protocol:** A document that describes the background, rationale, objectives, design,
1579 methodology, statistical considerations, and organization of a clinical research project. (Source:
1580 [UCSF Clinical Research Resource HUB](#)) A research protocol guides the study and associated
1581 data collection and analysis in a productive and standardized manner.

1582
1583 **Risk:** Risks are adverse events and other unfavorable effects associated with a medical product.
1584 Risks include drug interactions, risks identified in the non-clinical data, risks to those other than
1585 the patient (e.g., fetus, those preparing and administering the medical product), and risks based
1586 on pharmacologic class or current knowledge of the product. Factors such as potential misuse,
1587 abuse, or diversion of the product may also be considered. (Source: [International Conference on](#)
1588 [Harmonisation \(ICH\) Guidelines – Efficacy M4E\(R2\)](#))

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1590 **Risk tolerance:** The degree to which a patient would accept increased probability or severity of
1591 a harm in exchange for a specific expected benefit. (*Source: Medical Device Innovation*
1592 *Consortium (MDIC) [Patient Centered Benefit-Risk Project Report](#)*)
1593

1594 **Science of patient input:** Methods and approaches of systematically obtaining, analyzing, and
1595 using information that captures patients' experiences, perspectives, needs, and priorities in
1596 support of the development and evaluation of medical products.
1597

1598 **Social Media:** Web-based tools that are used for computer-mediated communication. Social
1599 media may include but is not limited to: (1) blogs, (2) microblogs, (3) social networking sites, (4)
1600 professional networking sites, (5) thematic networking sites, (6) wikis, (7) mashups, (8)
1601 collaborative filtering sites, (9) media sharing sites, and others. (*Source: [Grajales III et al. 2014](#)*)
1602

1603 **Subgroup:** A subset of the study population or study sample defined by specific baseline
1604 characteristics. For example, demographic subgroups are commonly defined by subject sex,
1605 race, and age.
1606

1607 **Surrogate endpoint:** A type of endpoint used in clinical trials as a substitute for a direct
1608 measure of how a patient feels, functions, or survives. A surrogate endpoint does not measure
1609 the clinical benefit of primary interest in and of itself but rather is expected to predict that
1610 clinical benefit or harm based on epidemiologic, therapeutic, pathophysiologic, or other scientific
1611 evidence. From a U.S. regulatory standpoint, surrogate endpoints and potential surrogate
1612 endpoints can be characterized by the level of clinical validation: (a) validated surrogate
1613 endpoints; (b) reasonably likely surrogate endpoints; and (c) candidate surrogate endpoints.
1614 (*Source: [BEST \(Biomarkers, Endpoints and Other Tools\) Resource](#)*)
1615

1616 **Target population** (also referred to as the *target patient population*, the *underlying population*,
1617 or *intended population*): The group of individuals (patients) about whom one wishes to make an
1618 inference.
1619

1620 **Trade-off:** The extent to which a change in the level of one or more attributes of a medical
1621 product that is offset by a change in one or more other attributes of that product. (*Source:*
1622 *Medical Device Innovation Consortium (MDIC) [Patient Centered Benefit-Risk Project Report](#)*)
1623

1624 **Treatment burden:** The impacts of a specific treatment or treatment regimen that have a
1625 negative effect on the patient's health, functioning, or overall well-being. Treatment burden
1626 includes (but is not limited to): side effects, discomfort, uncertainty about treatment outcomes,
1627 dosing and route of administration, requirements, and financial impacts.
1628

1629 **Treatment effect:** The amount of change in a disease/condition, symptom, or function that
1630 results from a medical intervention (as compared to not receiving the intervention or receiving a
1631 different intervention).
1632

1633 **Treatment outcome:** The benefits or harms to a patient who receives an intervention; the impact
1634 on a patient's health, function, or well-being—or on a clinical indicator thereof—that is assumed

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1635 to result from an intervention. (Source: *Patient-Centered Outcomes Research Institute (PCORI)*
1636 [Methodology Report](#))

1637

1638 **Unmet medical need:** An unmet medical need is a condition whose treatment or diagnosis is not
1639 addressed adequately by available therapy. An unmet medical need includes an immediate need
1640 for a defined population (e.g., to treat a serious condition with no or limited treatment) or a
1641 longer-term need for society (e.g., to address the development of resistance to antibacterial
1642 drugs). (Source: [FDA Guidance on Expedited Programs for Serious Conditions](#))

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1644 **APPENDICES**

1645

1646 Appendix 1: Methods for Collecting Patient Experience Data

1647 Appendix 2: Standards and Requirements Pertaining to Submission of Data

1648 Appendix 3: Considerations for Data Management

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1649 **Appendix 1. Methods for Collecting Patient Experience Data**

1650

1651 1. *Qualitative Research Methods*

1652

1653 Some aims of qualitative research are shown in [Table 7](#).

1654

1655 **Table 7. Qualitative Research Aims**

1656

Qualitative Research Aims ²⁰	Examples of potential research questions	Illustrative examples of qualitative data generation by question type
<i>To Understand ‘What’</i>	<ul style="list-style-type: none"> • What symptoms do heart failure patients experience? • What signs do caregivers observe that tell them their loved one is having asthma symptoms? • Based on your experience with COPD patients, what would you consider to be signs of severe COPD? 	<ul style="list-style-type: none"> • Patient #101: “I have trouble going up long flights of stairs.” • Caregiver #201: “I know my daughter is having a hard time with her asthma when she is wheezing.” • Clinician #301: “When a patient presents with typical symptoms and has had more than one COPD flare per year or if they have been hospitalized due to your COPD, I would consider them severe.”
<i>To Explore ‘Why’</i>	<ul style="list-style-type: none"> • Why are asthma symptoms bothersome to you? • Why do you prefer the auto-injector to intravenous (IV) injection? 	<ul style="list-style-type: none"> • Patient #101: “My asthma prevents me from being able to exercise without an inhaler.” • Patient #201: “The auto-injector is more convenient because I can administer it at home and it takes less time. My IV injections require a clinic visit and take hours.”
<i>To Examine ‘How’</i>	<ul style="list-style-type: none"> • How have arthritis symptoms impacted a patient’s mobility? • How has a patient’s dementia impacted the relationship dynamics in their family? • How have symptoms improved with treatment? 	<ul style="list-style-type: none"> • Patient #101: “My knees are stiff because of my arthritis. I find it hard to go up and down stairs.” • Caregiver #201: “My mom now requires 24-hour care. I’m often stressed about this and it’s putting a strain on my marriage.” • Patient #101: “Since receiving my lupus treatments, I’ve not

²⁰Note: any qualitative study could address one or more of these aims

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Qualitative Research Aims ²⁰	Examples of potential research questions	Illustrative examples of qualitative data generation by question type
		been in the hospital as much as before.”

1657 2. *Quantitative Research Methods*

1658

1659 [Table 8](#) summarizes some potential aims of quantitative research.

1660

Table 8. Quantitative Research Aims

1661

1662

Quantitative Research Aims	Examples of potential research questions	Examples of potential quantities of interest
<i>To Describe</i>	<ul style="list-style-type: none"> • How many (proportion of) patients experience stomach pain symptoms? • How frequently do epileptic patients experience seizures in a week? • How severe are patients’ heartburn symptoms? • Please rank your 3 most bothersome symptoms. 	Frequencies, proportions, means, medians, distributions
<i>To Compare</i>	<ul style="list-style-type: none"> • What is the difference in daily exacerbations among mild, moderate, and severe COPD patients? • To what extent do questionnaire responses differ among members of separate subgroups? 	Differences in frequencies, proportions, means, medians
<i>To Relate</i>	<ul style="list-style-type: none"> • What is the correlation between patient-reported sleep disturbance and actigraphy ratings? 	<ul style="list-style-type: none"> • Measures of association, trend, or interaction

1663

1664 3. *Software for Analyzing Quantitative Patient Experience Data*

1665

1666 Statistical software is available for analyzing quantitative patient experience data. Some
 1667 commonly used statistical software includes R, SAS, SPSS, and SUDAAN. SUDAAN, SAS,
 1668 STATA, and R are also commonly used to analyze survey data obtained from probability
 1669 sampling as each permits the specification of relevant design features such as clustering,
 1670 stratification, weights, and methods of variance estimation.

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1672 Regardless of which software you use, we recommend checking the current defaults and
1673 computational algorithms utilized as they vary both across software and across versions of the
1674 same software. Different estimation procedures and defaults may generate different results. In
1675 addition, be sure to note which software *version* was used as part of the study analysis
1676 documentation.

1677 **Appendix 2. Standards and Requirements Pertaining to Submission of Data**

1678
1679 Regulations, guidances, standards, and requirements pertaining to capture/collection,
1680 transmission, processing, storage, archiving, retention, and submission of data from clinical
1681 studies include (but are not limited to):

- 1682
- 1683 • FDA forms and submission requirements
1684 (<https://www.fda.gov/drugs/developmentapprovalprocess/formssubmissionrequirements/>)
1685
 - 1686 • The International Council on Harmonisation (ICH) Guidelines²¹, such as *ICH Harmonised*
1687 *Guideline for Good Clinical Practice: E6(R2)* and the *Electronic Common Technical*
1688 *Document (eCTD)*
1689
 - 1690 • 21 eCFR, Volumes 1 – 8²²
1691
 - 1692 • Guidance for Industry on Providing Regulatory Submissions In Electronic Format—
1693 Standardized Study Data (FDA, 2014b)
1694
 - 1695 • Guidance for Industry on Providing Regulatory Submissions in Electronic Format—
1696 Submissions Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act (FDA,
1697 2014a)
1698
 - 1699 • Guidance for Industry on Providing Regulatory Submissions in Electronic Format—Certain
1700 Human Pharmaceutical Product Applications and Related Submissions Using the eCTD
1701 Specifications (FDA, 2017)
1702
 - 1703 • Guidance for Industry on Electronic Source Data in Clinical Investigations (FDA, 2013)
1704
 - 1705 • The FDA Data Standards Catalog.
1706

1707 Current and more detailed information on study data standards resources, please see:
1708 <https://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/default.htm>.

²¹ <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>

²² https://www.ecfr.gov/cgi-bin/text-idx?tpl=/ecfrbrowse/Title21/21tab_02.tpl

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1709 **Appendix 3. Considerations for Data Management**

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Resources you may wish to consider when developing a data management plan include:

- Stanford University Libraries’ guide to DMPs (Stanford University Libraries, n.d.-b);
- The Society for Clinical Data Management’s (SCDM) standard for Good Clinical Data Management Practices (Society for Clinical Data Management, 2013); and
- Data management considerations laid forth in the National Science Foundation (NSF) Grant Proposal Guide Chapter II.C.2.j (NSF, 2014).

Components of good data management plans and practices include (NSF, 2014; Society for Clinical Data Management, 2013; Stanford University Libraries, n.d.-a):

- Having a complete draft of the DMP “prior to enrollment of the first study subject” and ensuring that “an approved, signed version of the DMP is completed prior to starting on the work it describes” (Society for Clinical Data Management, 2013);
- Ensuring “compliance with applicable regulations and oversight agencies” (Society for Clinical Data Management, 2013);
- Identifying and defining the “personnel and roles involved with decision making, data collection, data handling, and data quality control” (Society for Clinical Data Management, 2013);
- Ensuring “data management processes are described and defined from study initiation until database closeout” (Society for Clinical Data Management, 2013);
- Developing the DMP “in collaboration with all stakeholders to ensure that all responsible parties understand and will follow the processes and guidelines put forth in the DMP from study initiation to database closeout” (Society for Clinical Data Management, 2013);
- Developing and maintaining a DMP template that “ensures consistency and standardization across all projects” (Society for Clinical Data Management, 2013);
- Ensuring the DMP for each study is “kept current, including proper versioning, and that all responsible parties are aware of and agree to the current content” (Society for Clinical Data Management, 2013);
- Pre-specifying the types of data to be collected over the course of the study (NSF, 2014);
- Using standard, predetermined structure(s) for collecting patient experience data (e.g., interview scripts, questionnaire layouts, electronic devices, telephone prompts, etc.);

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- 1754 • Specifying “standards to be used for data and metadata format and content” (NSF, 2014);
1755
- 1756 • Using “descriptive and informative file names” (Stanford University Libraries, n.d.-a);
1757
- 1758 • Choosing “file formats that will ensure long-term access” to the data (Stanford University
1759 Libraries, n.d.-a);
1760
- 1761 • Having a systematic method for tracking different versions of datasets and documents (e.g.,
1762 data and metadata) (Stanford University Libraries, n.d.-a);
1763
- 1764 • Creating metadata for each analysis performed (Stanford University Libraries, n.d.-a);
1765
- 1766 • Having processes in place to ensure compliance with regulatory requirements of the
1767 protection and ownership of source data (Society for Clinical Data Management, 2013);
1768
- 1769 • Having policies in place for accessing and sharing data, including:
1770
 - 1771 ○ Provisions for appropriate protection of privacy, confidentiality, security, intellectual
1772 property, or other rights or requirements (NSF, 2014);
1773
 - 1774 ○ “Policies and provisions for re-use, re-distribution, and the production of derivatives”
1775 (NSF, 2014);
1776
- 1777 • Handling sensitive, confidential, and personally identifiable information and data in an
1778 appropriate manner, including ensuring an appropriate level of network and infrastructure
1779 security (Society for Clinical Data Management, 2013; Stanford University Libraries, n.d.-
1780 a); and
1781
- 1782 • Planning how data, samples, and other research products will be archived, and how access to
1783 these materials will be preserved for future access (NSF, 2014).
1784

1785 Other considerations and recommendations include:
1786

- 1787 • Data validation rules and electronic edit checks should be programmed to enhance data
1788 quality at the point of data entry. Prior to database lock, appropriate quality control
1789 measures should be taken to ensure that records with inconsistent values of variables (e.g.,
1790 age or gender) are identified, examined, and addressed.
1791
- 1792 • For observational studies, ensure proper logistics are in place to collect and manage data
1793 generated by follow-up queries, if needed. Variables should be cross-checked to verify
1794 subgroup assignment, subject disposition, reason for exclusion (where applicable), and type
1795 of error(s) detected in the record, if any.
1796

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- 1797 • Researcher(s) should design data management features to enhance data quality, minimize
1798 missing or erroneous data, and minimize data cleaning. In addition, use of customized error
1799 messages and automated data validations may facilitate survey completion.

1800

1801 If a research subject is excluded from an analysis, the reason for excluding the data collected
1802 from said subject should be thoroughly documented (and included in your submission to FDA).