



PATIENT-FOCUSED DRUG DEVELOPMENT
GUIDANCE PUBLIC WORKSHOP

**Methods to Identify What is
Important to Patients
&
Select, Develop or Modify
Fit-for-Purpose Clinical Outcomes
Assessments**

Workshop Date: October 15-16, 2018

1
2 **Attachment to Discussion Documents for Patient-Focused Drug**
3 **Development Public Workshop on Guidance 2 and 3:**
4 **METHODS TO IDENTIFY WHAT IS IMPORTANT TO**
5 **PATIENTS AND SELECT, DEVELOP OR MODIFY FIT-FOR-**
6 **PURPOSE CLINICAL OUTCOME ASSESSMENTS**
7
8 **LEGISLATION BACKGROUND (APPENDIX 1) and GLOSSARY**
9

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20 **APPENDIX 1. Legislation Background**

21

22 **A. Overview of the Series of FDA Guidance for Enhancing the Incorporation of the**
23 **Patient’s Voice in Drug¹ Development and Regulatory Decision Making**

24 This series of guidance documents builds on learnings from the disease-specific PFDD meetings²
25 that FDA conducted under the fifth authorization of the Prescription Drug User Fee Act (PDUFA
26 V) as an enhancement of the Agency’s implementation of a more structured approach to *benefit-*
27 *risk assessment*.³ The PFDD meetings conducted to date have given FDA a deeper appreciation
28 for the expertise that patients and caregivers can bring to the process and the value of
29 incorporating their voice. This series of guidance documents is intended to facilitate the
30 advancement and use of systematic approaches to collect and use robust and meaningful patient
31 and caregiver input that can better inform medical product development and regulatory decision
32 making.

33

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

41

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

43

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

45

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

50

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

53

54 *Guidance 2 will discuss methods for eliciting information from individuals identified in*
55 *Guidance 1, gathering information about what aspects of symptoms, impacts of their disease,*
56 *and other issues are important to patients. It will discuss best practices in how to do qualitative*
57 *research including conducting interviews, development of interview guides, selection of types*
58 *of survey questions, and considerations for collecting demographics and survey information. It*
59 *will also discuss survey methods and qualitative research topics to help avoid misleading*

¹ For the purposes of this document, all references to *drugs* include both human drugs and therapeutic biological products unless otherwise specified.

² <https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/ucm347317.htm>

³ <https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/ucm326192.htm>

60 *results such as inadvertently priming patients in ways that can lead to results that poorly*
61 *represent what is important to patients.*

62
63 **Guidance 3:** How do you decide what to measure in a clinical trial and select or develop ***fit-for-***
64 ***purpose clinical outcome assessments (COAs)***⁴?

65
66 *Guidance 3 will address refining the list of important impacts and concepts from patients to*
67 *develop potential study instruments. Given that not everything identified as important by*
68 *patients, caregivers, and clinicians can demonstrate change in a specific treatment trial or is*
69 *measurable, how will you select what to measure in a medical product development program to*
70 *show clinical benefit? How will you identify or develop fit-for-purpose COAs to assess*
71 *outcomes of importance to patients?*

72
73 **Guidance 4:** Once you have a COA measurement tool and a way to collect data using it, what is
74 an appropriate clinical trial endpoint?

75
76 *Guidance 4 will address topics related to COA-related endpoint development and*
77 *interpretation, including topics related to instrument administration and meaningful within-*
78 *patient score changes.*
79

80 **B. Patient Experience Data**

81 ***Patient experience data.*** Patient experience data is defined in Title III, Section 3002(b) of the
82 21st Century Cures Act as data intended to provide information about impact (including physical
83 and psychosocial impacts) of a disease or condition, or a related therapy or clinical investigation.
84 Patient experience data can be interpreted as including (but is not limited to) the experiences,
85 perspectives, needs and priorities of patients related to: 1) the symptoms of their condition and its
86 natural history; 2) the impact of the conditions on their functioning and quality of life; 3) their
87 experience with treatments; 4) input on which outcomes are important to them; 5) patient
88 preferences for outcomes and treatments; and 6) the relative importance of any issue as defined
89 by patients. For additional details on patient experience data, please refer to [Guidance 1](#).⁵
90 The following subsections will discuss patient experience data related to burden of disease and
91 treatment and benefits and risks in management of the patient’s disease.

92 93 *1. Burden of Disease and Treatment*

94
95 A disease or condition (hereon referred to as disease) generally has:

- 96 • a core set of distinctive signs and symptoms;
- 97 • affects specific groups of people; and
- 98 • follows a characteristic course.

⁴ Words or phrases found in the Glossary appear in bold italics at first mention within the body of text in this document.

⁵ *Draft Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders: Patient-Focused Drug Development: Collecting Comprehensive and Representative Input*

99 Diseases can be complex and have various consequences for patients which can affect its
100 measurement (Jones, Podolsky & Greene, 2012). For regulatory decision-making, there is a
101 need to understand the determinants of disease and treatment’s impact in patients’ lives to ensure
102 that the most meaningful outcomes are being measured in clinical trials.

103 ***Burden of disease and treatment.*** The burden of disease can be viewed as the impact of disease
104 on patients’ lives, from the onset of disease to the outcome of interest (e.g., disease severity,
105 disease improvement (recovery), or death). It may involve assessing the potential of treatment
106 (i.e., medical products) to change the disease course and future outcomes. For regulatory
107 purposes, FDA will view the burden of disease and treatment as the patient’s experience with the
108 disease and treatment from the patient’s perspective.

109 To evaluate the burden of disease and treatment, information should be gathered about how
110 diseases and treatments affect patients to provide a complete picture of the patient experience
111 (National Collaborating Centre for Infectious Diseases, 2016). Refer to **Section II** of the
112 Guidance 2 discussion document for details on the different methods on how to gather this
113 information.

114 Important aspects of burden that can characterize the patient’s experience, include but are not
115 limited to:

- 116 • the symptoms of patients’ disease and its natural history;
- 117 • the impact of the disease on their functioning and quality of life;
- 118 • patients’ experience with treatments;
- 119 • patient input on which outcomes are important to them;
- 120 • patient preferences for outcomes and treatments; and
- 121 • the relative importance of any issue as defined by patients.

122

123 *2. Benefits and Risks in Management of the Patient’s Disease*

124

125 ***Patient Engagement in Regulatory Benefit-Risk Assessments.*** To fully characterize patients’
126 experience with disease and treatment, it is important to understand how patients manage their
127 disease and their perspective on the benefits and risks in disease management.

128 Within medical product development, evidence should support that the benefits of using a
129 medical product for its intended use outweigh the potential risks. Weighing benefits and risks of
130 medical products requires the assessment of scientific evidence but also patient judgments about
131 the relative importance of benefits and risks.

132 To evaluate the patient’s perspective on benefits and risks in their disease management,
133 information should be gathered about what benefits or risks of are of interest to patients,
134 including degree of tolerability of adverse events to integrate patient concerns into regulatory
135 benefit-risk evaluations and complements the totality of impacts of disease and treatment. Refer
136 to **Section II of the Guidance 2 discussion document** for details on different methods on how
137 to gather this information.

138

139 **GLOSSARY**

140

141 As appropriate, definitions from existing federal resources (e.g., BEST (Biomarkers, Endpoints,
142 and Other Tools) Resource) have been incorporated into this glossary. External resources were
143 also utilized to define terms and have been cited.

144 **1. Ability to detect change:** Evidence that a COA can identify differences in scores over time
145 in individuals or groups who have changed with respect to the measurement concept.

146 **2. Assent:** A child’s affirmative agreement to participate in research capture through verbal and
147 written acknowledgement. Mere failure to object should not, absent affirmative agreement,
148 be construed as assent.

149
150 **3. Benefit:** Benefits are the favorable effects of a medical product. Types of benefit include
151 clinical benefit (*see definition below*). Benefits may also include important characteristics of
152 the medical product, such as convenience (e.g., a more convenient dosing regimen or route of
153 administration) that may lead to improved patient compliance, or benefits that affect those
154 other than the patient. (Source: [International Conference on Harmonisation \(ICH\)](#)
155 [Guidelines – Efficacy M4E\(R2\); ANSI/AAMI/ ISO 14971: 2007/\(R\)2016 Medical devices—](#)
156 [Application of risk management to medical devices](#))

157
158 **4. Benefit-risk assessment:** Evaluation of the demonstrated benefits and risks of a medical
159 product and making a judgment as to whether the expected benefits outweigh the potential
160 risks associated with its expected use.

161
162 **5. Caregiver:** A person who helps a patient with daily activities, health care, or any other
163 activities that the patient is unable to perform himself/herself due to illness or disability, and
164 who understands the patient’s health-related needs. This person may or may not have
165 decision-making authority for the patient and is not the patient’s healthcare provider.

166
167 **6. Ceiling effect:** A ceiling effect can occur at the item level or at the scale score level. An item
168 level ceiling effect is observed when a large concentration of participants endorses the
169 highest response category within an item. A scale score level ceiling effect is observed when
170 a large concentration of participants’ scores fall at or near the upper limit of the scale score of
171 the instrument. Either situation may occur when the upper extreme of the concept(s) assessed
172 by item response categories or by the scale score of the instrument does not
173 sufficiently match the level of the upper extreme of the target patient population.

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

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

179 **9. Clinical outcome assessment (COA):** Assessment of a clinical outcome can be made
180 through report by a clinician, a patient, a non-clinician observer or through a performance-

181 based assessment. Types of COAs include: patient-reported outcome (PRO) measures,
182 clinician-reported outcome (ClinRO) measures, observer-reported outcome (ObsRO)
183 measures, and performance outcome (PerfO) measures. (Source: *BEST (Biomarkers,*
184 *Endpoints and Other Tools) Resource*)

185 **10. Clinician-reported outcome (ClinRO):** A measurement based on a report that comes from a
186 trained health-care professional after observation of a patient's health condition. Most
187 ClinRO measures involve a clinical judgment or interpretation of the observable signs,
188 behaviors, or other manifestations related to a disease or condition. ClinRO measures cannot
189 directly assess symptoms that are known only to the patient (e.g., pain intensity). (Source:
190 *BEST (Biomarkers, Endpoints and Other Tools) Resource*)

191 **11. Cognitive interviewing:** A qualitative research process used to determine whether concepts
192 and items are understood by respondents in the same way that instrument developers intend.
193 Cognitive interviews involve incorporating follow-up questions in a field test interview to
194 gain a better understanding of how respondents interpret questions/tasks asked of them. In
195 this method, respondents are often asked to think aloud and describe their thought processes
196 as they answer the instrument questions. Respondents should reflect the target population
197 who will be responding to the instrument during the study.

198 **12. Concept (also referred to as concept of interest):** In a regulatory context, the concept is the
199 aspect of an individual's clinical, biological, physical, or functional state, or experience that
200 the assessment is intended to capture (or reflect). (Source: *BEST (Biomarkers, Endpoints*
201 *and Other Tools) Resource*)

202 **13. Concept elicitation:** A process or method to collect a holistic set of relevant concepts (i.e.
203 disease and treatment symptoms and associated impacts) that are important to patients from
204 relevant stakeholders (e.g., patients, experts, caregivers).

205 **14. Concept saturation:** When interviewing patients, caregivers, and/or experts, the point when
206 no new relevant or important information emerges and collecting additional data will not add
207 to the understanding of how patients perceive the concept of interest and the items in a
208 questionnaire.

209 **15. Conceptual framework:** An explicit description or a diagram for an instrument showing the
210 relationships between items (i.e., questions/tasks included in the instrument), domains (sub-
211 concepts), and concepts measured and the scores produced by a COA. The conceptual
212 framework of a COA evolves over the course of instrument development as empiric evidence
213 is gathered to support item grouping and scores.

214 **16. Construct validity:** Evidence that relationships among items, domains, and concepts
215 conform to a priori hypotheses concerning logical relationships that should exist with other
216 measures or characteristics of patients and patient groups.

217 **17. Content validity:** Evidence from qualitative research demonstrating that the instrument
218 measures the concept of interest including evidence that the items and domains of an
219 instrument are appropriate and comprehensive relative to its intended measurement concept,

- 220 population, and use. Testing other measurement properties will not replace or rectify
221 problems with content validity.
- 222 **18. Context of use:** A statement that fully and clearly describes the way the medical product
223 development tool is to be used and the medical product development-related purpose of the
224 use. (Source: *BEST (Biomarkers, Endpoints and Other Tools) Resource*)
- 225 **19. Criterion validity:** The extent to which the scores of a COA are related to a known gold
226 standard measure of the same concept. For most COAs, criterion validity cannot be measured
227 because there is no gold standard.
- 228 **20. Data analysis plan:** A roadmap for how the data will be organized and analyzed and how
229 results will be presented. A data analysis plan should be established when planning a
230 research study (i.e., before data collection begins). Among other things, the data analysis
231 plan should describe: (a) the data to be collected; (b) the analyses to be conducted to address
232 the research objectives, including assumptions required by said analyses; (c) data cleaning
233 and management procedures; (d) data transformations, if applicable; and (e) how the study
234 results will be presented (e.g., graphs, tables).
235
- 236 **21. Data management plan (DMP):** A written document that describes the data you expect to
237 acquire or generate during the course of your research study; how you intend to manage,
238 describe, analyze, and store said data; and what mechanisms you will use at the end of your
239 study to preserve and share your data. (Source: [Stanford University Libraries n.d.\(b\)](#))
240
- 241 **22. Disease burden:** The impacts, direct and indirect, of the patient’s health condition that has a
242 negative effect on his or her health, functioning, and overall well-being. Disease burden
243 includes (but is not limited to): the physical and physiologic impacts of the disease and its
244 symptoms; co-morbidities; emotional and psychological effects of the disease, its
245 management, or prognosis; social impacts; effects on relationships; impacts on the patient’s
246 ability to care for self and others; time and financial impacts of the disease and its
247 management; and considerations on the impacts on the patient’s family.
248
- 249 **23. Domain:** A subconcept represented by a score of an instrument that measures a larger
250 concept comprised of multiple domains. For example, psychological function is the larger
251 concept containing the domains subdivided into items describing emotional function and
252 cognitive function
- 253 **24. Endpoint:** A precisely defined variable intended to reflect an outcome of interest that is
254 statistically analyzed to address a particular research question. A precise definition of an
255 endpoint typically specifies the type of assessments made, the timing of those assessments,
256 the assessment tools used, and possibly other details, as applicable, such as how multiple
257 assessments within an individual are to be combined. (Source: *BEST (Biomarkers, Endpoints
258 and Other Tools) Resource*)
- 259 **25. Fit-for-purpose:** A conclusion that the level of validation associated with a tool is sufficient
260 to support its context of use. (Source: [BEST \(Biomarkers, Endpoints and Other Tools\)
261 Resource](#))

- 262 **26. Floor effect:** A floor effect can occur at the item level or at the scale score level. An item
263 level floor effect is observed when a large concentration of participants endorses the lowest
264 response category within an item. A scale score level floor effect is observed when a large
265 concentration of participants' scores fall at or near the lower limit of the scale score of the
266 instrument. Either situation may occur when the lower extreme of the concept(s) assessed by
267 item response categories or by the scale score of the instrument does not sufficiently match
268 the level of the lower extreme of the target patient population.
- 269 **27. Generalizability:** The extent to which study findings can be reliably extended to the target
270 population of interest.
- 271
- 272 **28. Instrument or tool:** An assessment system comprising three essential components: 1)
273 materials for measurement; 2) an assay for obtaining the measurement; and 3) method and/or
274 criteria for interpreting those measurements. (*Source: BEST (Biomarkers, Endpoints and*
275 *Other Tools) Resource*)
- 276 **29. Intended use:** The specific clinical circumstance or purpose for which a medical product or
277 test is being developed. In the regulatory context, "intended use" refers to the objective intent
278 of the persons legally responsible for the labeling of medical products. (*Source: BEST*
279 *(Biomarkers, Endpoints and Other Tools) Resource*)
- 280 **30. Item:** An individual question, statement, or task (and its standardized response options) that
281 is evaluated or performed by the patient to address a particular concept.
- 282 **31. Item tracking matrix:** A record of the development (e.g., additions, deletions,
283 modifications, and the reasons for the changes) of items or tasks used in an instrument.
- 284 **32. Health literacy:** The degree to which individuals have the capacity to obtain, process, and
285 understand basic health information and services needed to make appropriate health
286 decisions. (*Source: U.S. Department of Health and Human Services [Quick Guide to Health](#)*
287 *[Literacy](#)*) Health literacy also includes numeracy skills—such as calculating cholesterol and
288 blood sugar levels, measuring medication doses, and understanding nutrition labels—and
289 knowledge of health topics.
- 290 **33. Informed Consent:** The act of participants providing both verbal and written agreement to
291 participate in a research study. In order to facilitate the informed consent process, potential
292 participants must be provided with adequate information regarding the research study in an
293 understandable way that permits them to make an informed and voluntary decision about
294 whether or not to participate. The amount of information and the manner of presentation will
295 vary depending on the complexity and risk involved in the research study. Informed consent
296 is an ongoing educational interaction between the investigator and the research participant
297 that continues throughout the study. The requirement for informed consent is one of these
298 central protections defined by the:
- 299
- 300
- Department of Health & Human Services (HHS) regulations at [45 CFR part 46](#)
 - Food and Drug Administration (FDA) regulations at [21 CFR part 50](#)

- 301 **34. Labeling claim:** A statement of clinical benefit. A claim can appear in any section of a
302 medical product’s FDA-approved labeling or in advertising and promotional labeling of
303 prescription drugs, biologics, and devices.
- 304 **35. Literacy:** A person's ability to read, write, speak, and compute and solve problems at levels
305 necessary to: (a) function on the job and in society; (b) achieve one's goals; and (c) develop
306 one's knowledge and potential. (Source: U.S. Department of Health and Human
307 Services [Quick Guide to Health Literacy](#))
308
- 309 **36. Measurement properties:** All the attributes relevant to the application of a COA including
310 the content validity, construct validity, reliability, and ability to detect change. These
311 attributes are specific to the measurement application and cannot be assumed to be relevant
312 to all measurement situations, purposes, populations, or settings in which the instrument is
313 used.
- 314 **37. Methodologically sound:** Assurance that the methods and processes used to obtain and
315 analyze patient experience data are rigorous, robust, and adhere to scientifically established
316 principles and best practices for method development or implementation. Evidence generated
317 by methodologically sound methods and processes increases confidence that the results can
318 be trusted, interpreted, and support the intended regulatory uses.
319
- 320 **38. Mixed methods research:** Research that uses both qualitative and quantitative research
321 methods. See definitions for qualitative and quantitative research methods.
322
- 323 **39. Observer-reported outcome (ObsRO):** A measurement based on a report of observable
324 signs, events or behaviors related to a patient’s health condition by someone other than that
325 patient or a health professional. Generally, ObsROs are reported by a parent, caregiver, or
326 someone who observes the patient in daily life and are particularly useful for patients who
327 cannot report for themselves (e.g., infants or individuals who are cognitively impaired). An
328 ObsRO measure does not include medical judgement or interpretation. (Source: *BEST*
329 *(Biomarkers, Endpoints and Other Tools) Resource*)
- 330 **40. Patient:** Any individual with or at risk of a specific health condition, whether or not he or
331 she currently receives any therapy to prevent or treat that condition. Patients are the
332 individuals who directly experience the benefits and harms associated with medical products.
333
- 334 **41. Patient advocate:** An individual or group of individuals, who may or may not be part of the
335 target patient population, who has a role in promoting an interest or cause to influence policy
336 with respect to patients’ health or healthcare.
337
- 338 **42. Patient-centered:** See *patient-focused*
339
- 340 **43. Patient-centered outcome:** An outcome that is important to patients’ survival, functioning,
341 or feelings as identified or affirmed by patients themselves, or judged to be in patients’ best
342 interest by providers and/or caregivers when patients cannot report for themselves. (Source:
343 *ISPOR Plenary, [Patrick 2013](#)*)

- 344
- 345 **44. Patient engagement:** Activities that involve patient stakeholders sharing their experiences,
346 perspectives, needs, and priorities that help inform FDA’s public health mission. Such
347 activities may include (but are not limited to): testimony at Advisory Committee meetings,
348 submission to regulations.gov public docket; meetings attended by patients, FDA, and other
349 stakeholders; other correspondence with FDA; interactions through social media; and
350 interactions with or information from patient representatives or patient advocates.
351
- 352 **45. Patient experience data:** Defined in Title III, Section 3001 of the 21st Century Cures Act of
353 2016, as amended by section 605 of the Food and Drug Administration Reauthorization Act
354 (FDARA) of 2017,⁶ and includes data that are collected by any persons and are intended to
355 provide information about patients’ experiences with a disease or condition. Patient
356 experience data can be interpreted as information that captures patients’ experiences,
357 perspectives, needs, and priorities related to (but not limited to): 1) the symptoms of their
358 condition and its natural history; 2) the impact of the conditions on their functioning and
359 quality of life; 3) their experience with treatments; 4) input on which outcomes are important
360 to them; 5) patient preferences for outcomes and treatments; and 6) the relative importance of
361 any issue as defined by patients.
362
- 363 **46. Patient-focused** (also referred to as *patient-centered*): Ensuring that patients’ experiences,
364 perspectives, needs, and priorities are meaningfully incorporated into decisions and activities
365 related to their health and well-being.
366
- 367 **47. Patient-focused drug development (PFDD)** (also referred to as *patient-focused medical*
368 *product development*): A systematic approach to help ensure that patients’ experiences,
369 perspectives, needs, and priorities are captured and meaningfully incorporated into the
370 development and evaluation of medical products throughout the medical product life cycle.
371
- 372 **48. Patient input:** Information that captures patients’ experiences, perspectives, needs, and
373 priorities. See *Patient Experience Data*.
374
- 375 **49. Patient partner:** An individual patient, caregiver or patient advocacy group that engages
376 other stakeholders to ensure the patients’ wants, needs and preferences are represented in
377 activities related to medical product development and evaluation. (*Source: Wilson et al,*
378 *2018*)
379
- 380 **50. Patient perspective:** A type of patient experience data that specifically relates to patients’
381 attitudes or points of view about their condition or its management. Patient perspectives may

⁶ “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.” This definition is found in section 569C(c) of the FD&C Act (codified at 21 U.S.C. § 360bbb–8c), and is referred to in 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).

382 include (but are not limited to): perceptions, goals, priorities, concerns, opinions, and
383 preferences.
384

385 **51. Patient preference:** A statement of the relative desirability or acceptability to patients of
386 specified alternatives or choice among outcomes or other attributes that differ among
387 alternative health interventions. (Source: [FDA Guidance on PPI for medical devices](#))
388

389 **52. Patient-reported outcome (PRO):** A measurement based on a report that comes directly
390 from the patient (i.e., study subject) about the status of a patient's health condition without
391 amendment or interpretation of the patient's response by a clinician or anyone else. A PRO
392 can be measured by self-report or by interview, provided that the interviewer records only the
393 patient's response. Symptoms or other unobservable concepts known only to the patient
394 (e.g., pain severity or nausea) can only be measured by PRO measures. PROs can also assess
395 the patient perspective on functioning or activities that may also be observable by others.
396 (Source: *BEST (Biomarkers, Endpoints and Other Tools) Resource*)

397 **53. Patient representative:** An individual, who may or may not be part of the target population,
398 who has direct experience with a disease or condition (e.g., a patient or caregiver) and can
399 provide information about a patient's experience with the disease or condition.
400

401 **54. Performance outcome (PerfO):** A measurement based on a standardized task performed by
402 a patient that is administered and evaluated by an appropriately trained individual or is
403 independently completed.

404 **55. Qualitative research methods:** Methods associated with the gathering, analysis,
405 interpretation, and presentation of narrative information (e.g., spoken or written accounts of
406 experiences, observations, and events). Qualitative research methods may also include direct
407 observations (e.g., non-verbal communication and behaviors).
408

409 **56. Quantitative research methods:** Methods associated with the gathering, analysis,
410 interpretation, and presentation of numerical information.
411

412 **57. Recall period:** The period of time patients, caregivers, or clinicians are asked to consider in
413 responding to a COA item or task. Recall can be momentary (real time) or retrospective of
414 varying lengths.

415 **58. Reliability:** The ability of a COA to yield consistent, reproducible estimates of true treatment
416 effect.

417 **59. Representativeness:** Confidence that a sample from which evidence is generated is
418 sufficiently similar to the intended population. In the context of patient experience data,
419 representativeness includes the extent to which the elicited experiences, perspectives, needs,
420 and priorities of the sample are sufficiently similar to those of the intended patient
421 population.
422

- 423 **60. Research protocol:** A document that describes the background, rationale, objectives, design,
424 methodology, statistical considerations, and organization of a clinical research
425 project. (Source: UCSF [Clinical Research Resource HUB](#)) A research protocol guides the
426 study and associated data collection and analysis in a productive and standardized manner.
427
- 428 **61. Response scale:** The system of numbers or verbal anchors by which a value or score is
429 derived for an item. Examples include Likert scales, rating scales, visual analog scale (VAS).
- 430 **62. Risk:** Risks are adverse events and other unfavorable effects associated with a medical
431 product. Risks include drug interactions, risks identified in the non-clinical data, risks to
432 those other than the patient (e.g., fetus, those preparing and administering the medical
433 product), and risks based on pharmacologic class or current knowledge of the product.
434 Factors such as potential misuse, abuse, or diversion of the product may also be considered.
435 (Source: [International Conference on Harmonisation Guidelines – Efficacy M4E\(R2\),](#)
436 [ANSI/AAMI/ ISO 14971: 2007/\(R\)2016 Medical devices— Application of risk management to](#)
437 [medical devices](#))
438
- 439 **63. Risk tolerance:** The degree to which a patient would accept increased probability or severity
440 of a harm in exchange for a specific expected benefit. (Source: *Medical Device Innovation*
441 *Consortium (MDIC)* [Patient Centered Benefit-Risk Project Report](#))
442
- 443 **64. Science of patient input:** Methods and approaches of systematically obtaining, analyzing,
444 and using information that captures patients’ experiences, perspectives, needs, and priorities
445 in support of the development and evaluation of medical products.
- 446 **65. Score:** A number derived from a patient’s, caregiver’s, or clinician’s response to items or
447 tasks in an instrument. A score is computed based on a prespecified, appropriate scoring
448 algorithm and is subsequently used in statistical analyses of clinical trial results. Scores can
449 be computed for individual items, domains, or concepts, or as a summary of items, domains,
450 or concepts.
- 451 **66. Scoring algorithm:** A set of pre-specified rules to assign numerical value or values to
452 quantify the responses to the instrument. A scoring algorithm may create a single score from
453 a single item or multiple items (e.g., domain score).
- 454 **67. Sign:** Any objective evidence of a disease, health condition, or treatment-related effect. Signs
455 are usually observed and interpreted by the clinician but may be noticed and reported by the
456 patient.
- 457 **68. Social Media:** Web-based tools that are used for computer-mediated communication. Social
458 media may include but is not limited to: (1) blogs, (2) microblogs, (3) social networking
459 sites, (4) professional networking sites, (5) thematic networking sites, (6) wikis, (7) mashups,
460 (8) collaborative filtering sites, (9) media sharing sites, and others. (Source: [Grajales III et](#)
461 [al. 2014](#))
462
- 463 **69. Subgroup:** A subset of the study population or study sample defined by specific baseline
464 characteristics. For example, demographic subgroups are commonly defined by subject sex,

- 465 race, and age.
466
- 467 **70. Symptom:** Any subjective evidence of a disease, health condition, or treatment-related effect
468 that can be noticed and known only by the patient.
- 469 **71. Target population** (also referred to as the *target patient population*, the *underlying*
470 *population*, or *intended population*): The group of individuals (patients) about whom one
471 wishes to make an inference.
472
- 473 **72. Target product profile (TPP):** A clinical development program summary in the context of
474 labeling goals where specific types of evidence (e.g., clinical trials or other sources of data)
475 are linked to the targeted labeling claims or concepts.
- 476 **73. Task:** See *item*
- 477 **74. Treatment burden:** The impacts of a specific treatment or treatment regimen that have a
478 negative effect on the patient’s health, functioning, or overall well-being. Treatment burden
479 includes (but is not limited to): side effects, discomfort, uncertainty about treatment
480 outcomes, dosing and route of administration, requirements, and financial impacts.
- 481 **75. Treatment effect:** The amount of change in a disease/condition, symptom, or function that
482 results from a medical intervention (as compared to not receiving the intervention or
483 receiving a different intervention).
- 484 **76. Treatment outcome:** The benefits or harms to a patient who receives an intervention; the
485 impact on a patient’s health, function, or well-being—or on a clinical indicator thereof—that
486 is assumed to result from an intervention. (*Source: Patient-Centered Outcomes Research*
487 *Institute (PCORI) [Methodology Report](#)*)
- 488 **77. Usability testing:** A formal evaluation with documentation of respondents’ abilities to use
489 the instrument, as well as comprehend, retain, and accurately follow instructions.
- 490 **78. User acceptance testing (UAT):** One aspect of an extensive system/ software validation
491 process designed to determine whether the software complies with the written system
492 specification or user requirements document. It is not intended solely to determine if
493 respondents like or can use the system.
- 494 **79. Validation:** A process to establish that the performance of a test, tool, or instrument is
495 acceptable for its intended purpose. Elements of validation include but are not limited to the
496 following: construct validation, content validation, criterion validation, analytical validation,
497 clinical validation.
- 498