FDA | **U.S. FOOD & DRUG** ADMINISTRATION

PATIENT-FOCUSED DRUG DEVELOPMENT
PUBLIC WORKSHOP ON GUIDANCE 1

COLLECTING COMPREHENSIVE AND REPRESENTATIVE INPUT

ATTACHMENT TO DISCUSSION DOCUMENT

DRAFT STANDARDIZED NOMENCLATURE AND
TERMINOLOGIES FOR THE SERIES OF FDA
PATIENT-FOCUSED DRUG DEVELOPMENT (PFDD)
GUIDANCES (GLOSSARY)

Workshop Date: December 18, 2017

Overview

This draft glossary defines terms that will be used in the series of methodological Patient-Focused Drug Development (PFDD) FDA guidance documents that are required by the 21st Century Cures Act of 2016, and part of commitments made by FDA under the sixth authorization of the Prescription Drug User Fee Act (PDUFA VI). The goal of this draft glossary is to provide standardized nomenclature and terminologies related to patient-focused medical product development. The terms in this draft glossary have been defined specifically for the context of medical product development and regulatory decision making.

As appropriate, definitions from existing federal resources (e.g., BEST (Biomarkers, Endpoints, and Other Tools) Resource, FDA's COA Glossary of Terms, etc.) have been incorporated into this glossary. External resources were also utilized to define particular terms, and have been cited. FDA seeks feedback from patient stakeholders, researchers, medical product developers, and others on the draft glossary.

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

19 **Benefit:** See *clinical benefit*

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

105   **Patient:** Any individual with or at risk of a specific health condition, whether or not they
106   currently receive any therapy to prevent or treat that condition. Patients are the individuals who
107   directly experience the benefits and harms associated with medical products.

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

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

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

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

122 **Patient experience data:** Defined in Title III, Section 3002(c) of the 21st Century Cures Act of
123 2016[1] as data that are collected by any persons and are intended to provide information about
124 patients' experiences with a disease or condition. Patient experience data can be interpreted as
125 information that captures patients' experiences, perspectives, needs, and priorities related to (but
126 not limited to): 1) the symptoms of their condition and its natural history; 2) the impact of the
127 conditions on their functioning and quality of life; 3) their experience with treatments; 4) input
128 on which outcomes are important to them; 5) patient preferences for outcomes and treatments;
129 and 6) the relative importance of any issue as defined by patients.

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

133 **Patient-focused drug development (PFDD)** (also referred to as ***patient-focused medical***
134 ***product development***)**:** A systematic approach to help ensure that patients' experiences,
135 perspectives, needs, and priorities are captured and meaningfully incorporated into the
136 development and evaluation of medical products, throughout the medical product life cycle.

137 **Patient input:** Information that captures patients' experiences, perspectives, needs, and
138 priorities. See *Patient Experience Data.*

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

143 **Patient preference** *(noun)***:** A statement of the relative desirability or acceptability to patients of
144 attributes by which alternative health interventions may differ.

145 **Patient preference assessment:** An assessment using a patient preference method to assess
146 patient preference information (PPI).

147 **Patient preference information (PPI):** Assessments of the relative desirability or acceptability
148 to patients of specified alternatives or choices among outcomes or other attributes that differ
149 among alternative health interventions. *(Source: [FDA Guidance on PPI for medical devices](#))*

150 **Patient preference method:** Methods for assessing the relative desirability or acceptability of
151 attributes that differ among alternative diagnostic or therapeutic strategies. These methods may
152 be qualitative, quantitative, or mixed methods.

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[1] "(c) 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 or clinical investigation, on patients' lives; and (B) patient preferences with respect to treatment of such disease or condition."

153 **Patient-provided input:** *Patient experience data* or other information that comes directly from
154 patients.

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

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

166 **Performance outcome (PerfO):** A measurement based on a standardized task(s) performed by a
167 patient that is administered and evaluated by an appropriately trained individual or is
168 independently completed. These include measures of gait speed (e.g., timed 25 foot walk test),
169 memory recall (e.g., word recall test), or other cognitive testing (e.g., digit symbol substitution
170 test).

171 **Preference-sensitive decision:** Preference-sensitive decisions may occur when there is no option
172 that is clearly superior for all preferences. *(Source: FDA Guidance on PPI for medical devices)*

173 **Real world evidence (RWE):** Defined in Title III, Section 3022 of the 21st Century Cures Act of
174 2016 as "data regarding the usage, or the potential benefits or risks, of a drug derived from
175 sources other than randomized clinical trials." RWE is information about patient experience of a
176 medical product that is (a) applicable in real world settings, (b) derived from multiple sources
177 outside clinical research settings, (c) collected and analyzed using methods and processes that are
178 methodologically sound, and (d) fit-for-purpose in the regulatory context.

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

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

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

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

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

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

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

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

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

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

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

Treatment outcome: The benefits or harms to a patient who receives an intervention; the impact on a patient's health, function, or well-being—or on a clinical indicator thereof—that is assumed to result from an intervention.*(Source: Patient-Centered Outcomes Research Institute (PCORI) Methodology Report)*