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)

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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.

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

Benefit: See ***clinical benefit***

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

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

Caregiver: 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.

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

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

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

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

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

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

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

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

Patient: 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.

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

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

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

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

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

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

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

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

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

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

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

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

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

[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."

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

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

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

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

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

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

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

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