



Patient-Focused Drug Development – Recommended Language for Use in Guidance Document Development

This document was prepared by the National Health Council and Genetic Alliance with the intent of submission to the Food and Drug Administration to encourage adoption, wholly or in part, by the Agency.

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Patient-Focused Drug Development – Recommended Language for Use in Guidance Document Development

First in a Series of Recommended Guidance Documents for Food and Drug Administration Consideration

Purpose of this document:

1. The National Health Council (NHC) and Genetic Alliance (GA) have been dedicated to furthering patient engagement in drug development and hosted three multi-stakeholder events to inform the development of draft guidance document language, language that could be offered to the Food and Drug Administration (FDA or the Agency) to help advance its work in this area. This document reflects the NHC and GA language recommendations for FDA consideration in future patient engagement guidance documents.

Objectives for the recommended language offered in this document:

1. Convey to the public that the Food and Drug Administration supports and encourages, but does not require, patient-focused drug development activities.
2. Provide definitions for the various terms used related to patient-focused drug development to encourage standardization.

Recommended Language

I. Introduction

Patient input during drug¹ product research, development, review, and post-marketing evaluation is critical to the development and life-cycle management of treatments that meet patient needs, enhance the research and approval processes, and improve patient outcomes. Historically, FDA has sought input from patients who serve as members on FDA Advisory Committees² and during sponsor meetings discussing specific products. This document supports the Agency's focus on

¹ The term drug as used in this guidance refers to both human drugs and biological products unless otherwise specified.

² See FDA website, About the Patient Representative Program, (<http://www.fda.gov/ForPatients/About/ucm412709.htm>) (last visited February 16, 2016).

expanding and formalizing the collection and use of patient input through the Patient-Focused Drug Development (PFDD) initiative³ and providing a more structured benefit-risk framework.⁴

FDA values the perspectives of patients and is committed to encouraging patient input throughout drug development and product reviews.⁵ The Agency recognizes patients as experts and believes patients can bring their experiences to bear to enhance regulatory decision-making.

FDA's guidance documents, including draft guidance that might include this language, do not establish legally enforceable responsibilities. Instead, they describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word "should" in Agency guidance means that something is suggested or recommended, but not required.

II. Background

Patient-provided information (PPI) is an important, and necessary, component in drug development and product review. For example, the insights that patients provide on a range of topics, from their experience living with their disease to their priorities for treatment outcomes, helps sponsors ensure that their products meet the needs of patients and helps FDA assess a product's benefits and risks. For sponsors to obtain this insight, they need to engage in non-promotional interactions with patients for research purposes. These interactions are appropriate, though they are set by different guidelines and intended to provide sponsors with patient insights that are integral to successful drug development and product review.

In 2012, Congress passed the Food and Drug Administration Safety and Innovation Act (FDASIA), which included provisions to enhance patient engagement in drug development and product reviews,⁶ such as section 1137, which required FDA "to develop and implement strategies to solicit the views of patients during the medical product development process and consider the perspectives of patients during regulatory discussions."⁷ Since that time, patients have had a growing number of opportunities to become involved in drug development and product review, including serving on FDA Advisory Committees, providing input during specific product meetings with sponsors, and participating in FDA's PFDD meetings.

A. What is "patient-provided information"?

For the purposes of this guidance, "patient-provided information" describes information a patient contributes directly at any point during the product lifecycle. As defined in Section III, the term broadly encompasses the entirety of information that can be collected from an interaction with a patient. Section IV also provides definitions for other similar terms and describes their

³ See Prescription Drug User Fee Act V Patient-Focused Drug Development; Consultation Meetings; Request for Notification of Patient Stakeholder Intention To Participate, 77 Fed. Reg. 58848 (Sept. 24, 2012).

⁴ See FDA website, Enhancing Benefit-Risk Assessment in Regulatory Decision-Making, (<http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm326192.htm>) (last visited February 11, 2016).

⁵ See also for CDRH, FDA's *Guidance for Industry and Food and Drug Administration Staff; Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications* issued on March 28, 2012 (<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM296379.pdf>); see also FDA's *Draft Guidance for Industry, Food and Drug Administration Staff; and Other Stakeholders; Patient Preference Information – Submission, Review in PMAs, HDE Applications, and De Novo Requests, and Inclusion in Device Labeling* issued on May 18, 2015 (<http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm446680.pdf>).

⁶ See Food and Drug Administration Safety and Innovation Act (FDASIA), Pub. L. 112-144, 126 Stat. 993 (2012).

⁷ See FDASIA § 1137.

relationship relative to one another. The focus should be the patients view on their disease(s)/condition(s), desired attributes for treatments, experiences with treatments, benefit-risk preferences, and desired goals and outcomes. It should not be primarily focused on any one product.

PPIIn includes, but is not limited to, information from patients about:

- the natural history of the disease
- the impact of the disease or condition on patients and their family caregivers, and how it affects their daily activities, physical functions, and quality of life
- outcomes that are most important to the patient, both clinical and non-clinical (e.g., goals for daily activities, symptom reduction, or a standard of quality of life)
- patients' preferences for treatment delivery methods and opinions about side effects
- experience on treatment(s) including symptoms and side effects and how the treatment impacts their daily activities, physical functions, and quality of life

As illustrated by this list, PPIIn covers a wide variety of input from the patient regarding the patient's experience, preferences, and needs. However, PPIIn does not include all information obtainable about a patient. For example, pathology results are "patient information" and distinct from PPIIn because they are not conveyed directly by the patient.

B. What are FDA's PFDD initiative and patient-focused drug development?

FDA's PFDD initiative, a commitment under the fifth authorization of the Prescription Drug User Fee Act (PDUFA V), has allowed the Agency to more systematically gather patients' and family caregivers' perspectives on living with a disease, the symptoms that matter most to them, and their experiences with available therapies.⁸ As part of this initiative, FDA has committed to holding public meetings, each focusing on a specific disease area.⁹ FDA summarizes the input it receives during these meetings in a publicly reported series entitled, "Voice of the Patient."¹⁰ The information provided by patients at these meetings is critical to the Agency's understanding of the needs and preferences of patients diagnosed with these diseases. FDA can use this patient input to inform the Agency's regulatory decision-making, especially when assessing a product's benefit-risk profile. For diseases for which a formal FDA PFDD meeting is not planned, FDA recommends patient groups consider holding their own, external PFDD meetings and has provided insights on how to do so.¹¹

FDA's PFDD initiative represents just one way in which PPIIn can be integrated into the product lifecycle. The broader term "patient-focused drug development" refers to meaningful engagement of patients throughout the product lifecycle, from the early stages of discovery to post-market studies, and extends beyond the Agency's recent activities.

⁸See Footnote 12 *Patient-Focused Drug Development: Disease Area Meetings Planned for Fiscal Years 2013-2017*, <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm347317.htm> (last visited February 16, 2016).

⁹See Footnote 12 *Patient-Focused Drug Development: Disease Area Meetings Planned for Fiscal Years 2013-2017*, <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm347317.htm> (last visited February 16, 2016).

¹⁰ See *The Voice of the Patient: A Series of Reports from FDA's Patient-Focused Drug Development Initiative*, <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm368342.htm> (last visited February 16, 2016).

¹¹ See *Externally-led Patient-Focused Drug Development Meetings*, <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm453856.htm> (last visited February 16, 2016).

C. Who is involved in patient-focused drug development?

In general, the exchange that takes place during patient interactions to collect patient-provided information involves:

Those *gathering patient-provided information*, which can include, but is not limited to, sponsors, academic researchers, health care providers, professional societies, special interest groups, patient groups, FDA, and those contracted to collect information or act as an intermediary between another entity and patients.

Those *providing patient-provided information*, which can include, but is not limited to, individual patients, family caregivers, individual patient advocates, or patient advocacy organizations (defined as “patients”, see Section IV).

The context of a particular patient interaction (e.g., the objectives and format of the interaction; the point in product development in which the interaction occurs) informs which entities are involved in a particular interaction or series of interactions with patients. For example, in the context of designing clinical trials for a particular drug, the sponsor of that drug will generally be the primary entity collecting PPI. FDA may also collect PPI at many points before and during drug development. Patient interaction during drug development is not limited to sponsors and FDA; academic researchers, professional societies, or patient advocacy organizations may also gather PPI to inform their own and others research efforts. Guidance may encourage the use of PPI in PFDD by all stakeholders.

The provider of PPI also will vary depending on the circumstance. For example, family caregivers may provide information on behalf of children or patients who may not have the capacity to engage. Family caregivers may also engage in lieu of individual patients to provide the specific perspective of the caregiver. Similarly, patient advocacy organizations can provide a perspective that uniquely captures the heterogeneity of a patient population. They also may act as a key conduit for sponsors or researchers seeking to engage with a particular patient population.

FDA recognizes that patients can assume different roles in these engagements. Patients can serve as advisors or consultants to provide input on research questions, study designs, or patient engagement plans. In addition, patient interactions can be formal or informal. Formal interactions may include arrangements that stipulate roles, responsibilities, any contractual obligations of the parties, as well as compensation. Informal interactions may consist of brief or temporary engagements (e.g., patients responding to a survey).

D. Why include patient-provided information in disease research and drug development?

Draft guidance may include language recognizing the value of PPI to those who are conducting disease research and drug development. Understanding from patients their experience of living with a disease over time is critical to, for example, understanding the natural history of a disease and identifying unmet medical needs. In addition, PPI can identify the symptoms of a disease that are most bothersome to patients, the clinical outcomes patients care most about, ways to make a clinical trial less burdensome to patients, and treatment characteristics patients prefer. If integrated into decision-making and product planning, this

information can help product sponsors develop drugs that align with patient preferences and needs, and gather outcome data patients care about.

Patients can advise on any number of drug-development challenges to help ensure new drugs better meet patient needs and goals and enhance patient outcomes. Guidance may include language to encourage sponsors and other involved stakeholders to engage patients early and continuously in the drug development process to prevent avoidable misalignment between patient needs and preferences and development decisions and processes. This will help ensure study protocols reflect patient input, and the data captured are important to patients. In addition, early engagement can help produce product labeling that includes information important and understandable to patients.¹²

Sponsors and other stakeholders can better understand the heterogeneity of patient perspectives by engaging patients. Knowledge about how a disease impacts patients across age, disease severity, and disease progression (e.g., newly diagnosed or having lived with the disease for decades), as well as the heterogeneity of treatment effects across patients, can also inform drug development.

Many of the approaches and considerations for engaging patients can also be more broadly applied to research and development processes for all medical products, as well as basic disease-specific research (e.g., natural history studies). PPI can provide value to all clinical research, and researchers should consider meaningfully engaging patients to support their studies in general.

III. Overview and Scope

This document provides FDA with recommended language of current perspectives on PPI. This language applies in general, unless otherwise stated, to engagement with patients with regard to a disease, condition, or therapeutic area. In many instances, patient engagement happens unrelated to any specific product or products. When it does relate to a product or products, it can include research prior to discovery or development and the complete lifecycle of a drug (the “product lifecycle”). Research prior to discovery or development includes studies on the natural history of disease and identifying unmet medical need, and is typically disease- or therapeutic-area focused. It may not include any reference to any treatments as it may be too early in the development process for such discussion. The product lifecycle includes the discovery, research, and development tied to a specific product (e.g., clinical trials to demonstrate safety and efficacy of the product); regulatory review of that product for market approval or licensure; and post-approval study and development of that product (e.g., post-marketing commitments, surveillance that continues for as long as a product is available, or submission for new indications). There are nuances that differentiate the types of engagement needed throughout the product lifecycle. In this document, the term “product lifecycle” encompasses this full timeline, pre-product and post-approval. In this document, the word “research” refers to all phases of research from pre-product to post-approval, and therefore, includes research about the disease or therapeutic area alone, with or without reference to treatment.

¹² See Footnote 5 *Draft Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders; Patient Preference Information – Submission, Review in PMAs, HDE Applications, and De Novo Requests, and Inclusion in Device Labeling.*

This document recommends definitions of the principal concepts and key terms related to engaging patients outside of and during the product lifecycle. Information provided by patients during these interactions may inform FDA's thinking on a disease, condition, or therapeutic area, such as understanding the impact a disease has on patients' lives and the outcomes that are important to patients with that disease. It may also inform FDA premarket review of Investigational New Drug Applications (INDs), New Drug Applications (NDAs), Supplemental New Drug Applications (sNDAs), Biologics License Applications (BLAs), Supplemental Biologics License Applications (sBLAs), Investigational Device Exemption (IDEs), Premarket Approval (PMAs), (sPMAs) and ongoing safety surveillance.

Submission of PPI to FDA is voluntary. The information submitted should inform decision making. PPI can be useful to, among other things:

- Identify unmet medical need;
- Understand the natural history of a disease;
- Identify outcomes that patients care about;
- Develop clinical trial protocols that minimize burden to patients;
- Understand patient experiences with current treatments and daily living with their disease;
- Identify patient preferences, goals, and opinions, including those of a diverse patient population (and the heterogeneity within);
- Identify with which benefits and risks outcomes matters most to patients and the tradeoffs patients are willing to make between benefits and risks; and
- Refinement of materials such as informed consent, clinical trial recruitment materials, patient information leaflets, package inserts, PLS, etc.

This document recommends that FDA encourage product sponsors and other stakeholders to meaningfully engage patients throughout the product lifecycle. This document recommends the Agency welcomes submission of PPI from sponsors and other stakeholders, and engage in a dialogue with the relevant review division on PPI. This document, including the defined terminology, may be informative to other stakeholders, including patient groups and academic researchers, who collect and submit PPI to the FDA. This document recommends the Agency encourages sponsors and other stakeholders that are considering PPI for submission to FDA to communicate with the relevant FDA review division to discuss their plans for patient engagement as early in the process as possible. The next section consists of NHC recommendations to define key terms related to patient-focused drug development.

IV. Defining Key Terms for Patient Engagement

Patient engagement, in drug development and product review, means involving patients as active participants in these processes. Simply enrolling and following patients as passive research subjects in a clinical trial does not rise to the level of patient engagement. Instead, patients should be treated “as valued and valuable partners whose input, advice, and guidance is sought and implemented” throughout these processes.¹³ FDA recognizes that patient engagement extends well beyond drug development and approval. However, for the purposes of this document, the focus is on patient engagement prior to and throughout a product's lifecycle.

¹³ A. Hoos A, *et.al.*, “Partnering with Patients in the Development and Lifecycle of Medicines: A Call for Action,” *Therapeutic Innovation & Regulatory Science*, (2015).

FDA recognizes the need for standard terminology regarding patient engagement in drug development and approval. Key terms are defined or described for the purposes of this guidance as follows:

Patient – “those (people) having or at risk of having the medical condition(s) whether or not they currently receive medicines or vaccines to prevent or treat a disease” as well as “the family and those caring for those with the medical condition(s),” patient advocates, and patient groups.¹⁴

The definition of “patient” is intentionally broad in an effort to capture the myriad of valuable input to be gained from each of the listed individuals and organizations (i.e., individuals suffering from a condition, family caregivers, patient advocates, and patient advocacy organizations) without excluding a valuable perspective. However, we recognize that each type of individual or organization may not always be appropriate to speak for the person with the condition in all contexts and situations. When this guidance refers to the single person with the illness, the phrase, “individual patient,” is used.

Sponsor – an entity that takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or pharmaceutical company, a government agency, academic institution, private organization, or other organization.¹⁵ The sponsor may also be the entity responsible for submitting a new product application for FDA review.¹⁶

There are many terms to describe different types of patient information. For the purposes of this document, it is recommended FDA focuses on **patient-provided information (PPI)**, defined below. To distinguish patient-provided information for the purposes of this guidance, other types of **patient information** are defined as follows (see also Figure 1 on page 11):

Patient information – broadly means all information regarding a patient from any source, such as patient-provided information as well as other medical information about a patient, including but not limited to: test results (e.g., genetic, pathology, imaging), identifying information, family history, provider opinion, and any other information in a patient’s medical records.¹⁷

Patient-provided information (or patient-provided input) – broadly means a range of information that comes directly from patients such as, but not limited to: views, experiences, preferences, needs, opinions, and priorities. This can include their overall view of their condition and its natural history and impact on their life (e.g., patient-reported outcomes such as symptoms, function, and quality of life); experience with available treatments; description/view on which outcomes are important; patient preferences, goals, desires, concerns, perceptions, or opinions; or the relative importance of any issue as defined by patients.¹⁸ *Patient-provided is information relayed by the patient regarding their subjective experience and opinions.* It does not include all

¹⁴ See Footnote 6.

¹⁵ See 21 CFR 312.3(b).

¹⁶ See 21 CFR 314.3(b).

¹⁷ National Health Council, Genetic Alliance. Integrating the Patient into the Drug Development Process: Developing FDA Guidance, (<http://www.nationalhealthcouncil.org/sites/default/files/NHC-GA-Patient-Engagement.pdf>).

¹⁸ See Footnote 10 National Health Council, Genetic Alliance. Integrating the Patient into the Drug Development Process: Developing FDA Guidance, (<http://www.nationalhealthcouncil.org/sites/default/files/NHC-GA-Patient-Engagement.pdf>)

medical information on a patient (e.g., genetic testing information, pathology results) that may be about the patient but comes from other sources.

Patient-generated health data – health-related data created, recorded, or gathered by or from patients (or family members or other caregivers) to help address a health concern.¹⁹

Patient perspective information – a subset of PPI; information regarding the attitude or the point of view of the patient, including anecdotal comments in correspondence to FDA or testimony at Advisory Committee Panel meetings²⁰ or Patient-Focused Drug Development meetings,²¹ patient opinions expressed publicly including through social media, patient responses to qualitative, *ad hoc* surveys, quantitative measurements of patient-reported outcomes, and more.^{22,23}

Patient preference information – a subset of PPI; qualitative or quantitative assessments of the relative desirability, or acceptability of, attributes that differ among alternatives (e.g., alternative therapeutic strategies).²⁴ Attributes of a drug or biologic include characteristics such as effectiveness, safety, route of administration, dosing regimens, duration of effect, duration of use, and other product features about which patients express preferences.

Patient-reported information – a subset of PPI; information that is reported directly by a patient without amendment or interpretation by a clinician, researcher, or any other entity.²⁵

Patient-reported outcome (PRO) – a subset of PPI; an outcome measure based on a report that comes directly from the patient (e.g., study subject) about the status of the 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 responses.²⁶

¹⁹See patient-generated health data, *HealthIT.gov website, Consumer eHealth*, <https://www.healthit.gov/policy-researchers-implementers/patient-generated-health-data> (last visited April 8, 2016).

²⁰ See Footnote 2 See FDA website, *About the Patient Representative Program*, (<http://www.fda.gov/ForPatients/About/ucm412709.htm>) (last visited February 16, 2016).

²¹ See Patient-Focused Drug Development: Disease Area Meetings Planned for Fiscal Years 2013-2017, <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm347317.htm> (last visited February 16, 2016).

²² See Footnote 5 *Draft Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders; Patient Preference Information – Submission, Review in PMAs, HDE Applications, and De Novo Requests, and Inclusion in Device Labeling*.

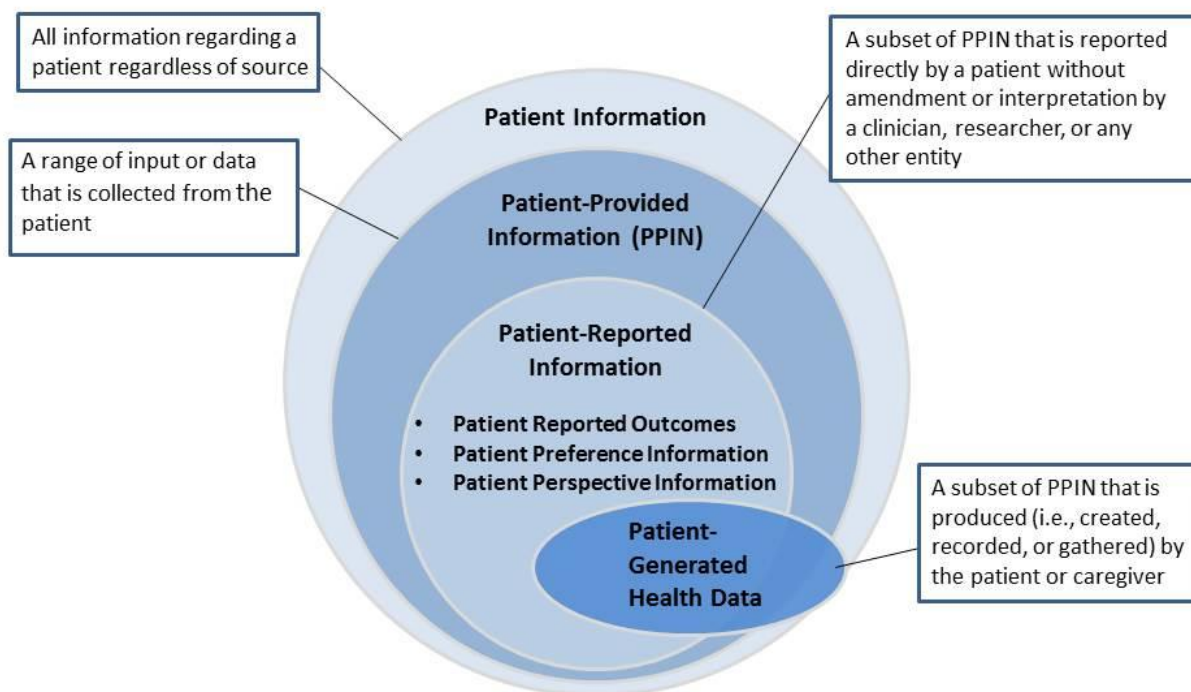
²³ See FasterCures, *Enhancing Integration of Patient Perspective Data in the Drug Development Process, Proposal for PDUFA VI*, (<http://www.nationalhealthcouncil.org/sites/default/files/FasterCures-PDUFA-Comment-Letter-FDA.pdf>).

²⁴ See Footnote 5 *Draft Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders; Patient Preference Information – Submission, Review in PMAs, HDE Applications, and De Novo Requests, and Inclusion in Device Labeling*.

²⁵ See Footnote 10.

²⁶ See the guidance for industry, *Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims* (<http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm193282.pdf>). For the most recent version of a guidance, check the FDA Drug guidance Web page at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm> (last visited February 16, 2016).

Figure 1: Relationship Among Types of Patient Information



Key terms are defined or described for the purposes of inclusion in a draft guidance document as follows:

Patient voice – broadly refers to capturing and utilizing PPI.²⁷

Patient involvement – broadly refers to patient participation or contribution in a process.²⁸

Patient engagement/interaction – a specific reciprocal action between a patient or patients and another individual or group for the purposes of collecting PPI from the patient and/or communicating with the patient. Can be formal or informal; direct or indirect (i.e., through a third party such as a patient group).²³ Meaningful patient engagement requires other attributes such as continuous patient interactions on a sustained basis. (See meaningful patient engagement.)

²⁷See NHC comments on FDA's Draft Guidance on Patient Preference Information, (<http://www.nationalhealthcouncil.org/sites/default/files/Patient-Preference-FDA-Guidance-Comments.pdf>).

²⁸See also: *Patient involvement in the European Union*, http://ec.europa.eu/dgs/health_consumer/dyna/enews/enews.cfm?al_id=1259.

Patient risk tolerance – A qualitative term reflecting the extent to which a patient will accept the risk(s) of an adverse effect from a treatment for a probable benefit; risk tolerance will vary among patients, which affects individual patient decisions as to whether risks are acceptable.²⁹

Meaningful patient engagement – Interactions intended to inform decision making that include direct relationships and partnerships with patients that are bidirectional, reciprocal, and continuous; where communications are open, honest, and clear; and where engagement goals, participants, methods, desired impacts, and actual impacts are clearly outlined and transparent.³⁰

Patient need – a desire or requirement expressed by a patient related to their health.²³

Patient-centered – broadly meaning any process, program or decision focused on patients in which patients play an active role as meaningfully engaged participants, and the central focus is on optimizing use of PPI.³¹

Patient-informed drug development – generally refers to drug development that uses PPI to guide or inform decisions but may or may not include patient involvement.³²

Patient-focused drug development (or patient-directed drug development or patient-focused medicines development) – is the meaningful engagement of patients in the research and development of therapeutic products and the various important roles patients can play in improving the processes, from study endpoint selection that reflects outcomes meaningful to patients, recruitment and retention in clinical trials, and more effective post-marketing safety surveillance.³³

Patient-Focused Drug Development (PFDD) initiative – refers specifically to FDA’s patient-focused drug development initiative as part of FDA commitments under the fifth authorization of the Prescription Drug User Fee Act (PDUFA V), which aims to more systematically obtain the patient perspective on specific diseases and their treatments.³⁴

Product Lifecycle – the entire product development process; research prior to discovery, development, or preference, pre-product research, and throughout the complete to post approval.³⁵

The terminology and concepts described here also may be useful in other contexts. Additionally, this document may be informative to other stakeholders who may wish to consider engagement with patients to inform any type of medical product development.

²⁹ See CDRH guidance for industry, *Factors to Consider Regarding Benefit-Risk in Medical Device Product Availability, Compliance, and Enforcement Decisions*,

<http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm506679.pdf> (last visited November 7, 2016).

³⁰ See National Health Council. The Patient Voice in Value: The National Health Council Patient-Centered Value Model Rubric, <http://www.nationalhealthcouncil.org/sites/default/files/Value-Rubric.pdf>.

³¹ Epstein RM, Street RL. The Values and Value of Patient-Centered Care. *Annals of Family Medicine*. 2011;9(2):100- 103. doi:10.1370/afm.1239.

³² See Footnote 10 National Health Council and Genetic Alliance. Integrating the Patient into the Drug Development Process: Developing FDA Guidance. (<http://www.nationalhealthcouncil.org/sites/default/files/NHC-GA-Patient-Engagement.pdf>).

³³ See Clinical Trials Transformation Initiative, CTTI Recommendations: Effective Engagement with Patient Groups Around Clinical Trials, <http://www.ctti-clinicaltrials.org/files/PatientGroups/PGCTrecs.pdf> (last visited February 16, 2016).

³⁴ See Footnote 3.

³⁵ See Footnote 20 NHC comments on FDA’s Draft Guidance on Patient Preference Information, (<http://www.nationalhealthcouncil.org/sites/default/files/Patient-Preference-FDA-Guidance-Comments.pdf>).