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ASSESSING MEANINGFUL PATIENT ENGAGEMENT IN DRUG DEVELOPMENT: A DEFINITION, FRAMEWORK, AND RUBRIC

Deliverables from conference organized by the University of Maryland Center of Excellence in Regulatory Science and Innovation (CERSI), government agencies, academia, and industry to provide a forum for all patient-focused drug development stakeholders to gather for an open dialogue.

Assessing Meaningful Patient Engagement in Drug Development: A Definition, Framework, and Rubric

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Key words: Patient-centered, patient engagement, patient focused, patient involvement, drug development, drug approval; regulatory review; reimbursement; PDUFA

Abstract

A movement to include the patient voice in health care research and decision making is underway. In light of broad stakeholder interest in patient-focused drug development (PFDD), a range of stakeholders are considering approaches to increase the scope of PFDD and enhancing patient engagement. On March 9, 2015, the University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI), with the support of many partner organizations, held the “M-CERSI Conference on Patient-Focused Drug Development.” The objective was to allow stakeholders from patient groups, the US Food and Drug Administration (FDA), the biopharmaceutical industry, payer, and other organizations to voice their views on, activities in, and aspirations for PFDD. During the day-long program, participants discussed the challenges to successful PFDD including regulatory challenges, the patient and patient advocate role, the emerging payer role, along with future directions and opportunities for collaboration. This document summarizes the outputs of the conference including a suggested definition, rubric, and framework for PFDD.

Definition for PFDD

All stakeholders agreed that the time has come for PFDD. However, a clear definition of PFDD and patient engagement in drug development are needed. It was discussed that PFDD is a process by which we bring new medicines to market, informed at every step of the path by input from persons living with the disease. Patient engagement does not end with product approval; patients also play a key role in ensuring access, defining value, and informing disease management and adherence programs. Patient engagement is a mindset and a framework; it extends beyond the regulatory process. The PFDD process does not end after a drug receives regulatory approval; patients and stakeholders need to be engaged throughout the entire life cycle.

It was also discussed that these efforts are not limited to drug development. PFDD extends beyond drugs to all treatments and diagnostics. The concepts discussed also apply to the development and testing of other medical products such as medical devices and diagnostics. Thus, conceptually, we should be broadening the definition to consider patient centeredness in medical product development in general.

Conference participants expressed concern that perhaps the word “patient” is not correct or is too limiting. Suggestions included “person” or “people,” however, no consensus was reached on this point. It is important to note that when the word “patient” is used in the context of PFDD more generally, it often is intended to include others such as caregivers, family members, those at risk for a disease, etc. as contextually applicable.

With these discussions in mind, a proposed definition for patient-focused drug or medical product development is:

Patient-focused drug development is a formal process by which drug developers and regulators form a partnership with the patient to enhance drug* development, research, regulatory, and reimbursement processes with the patient voice. This partnership engages patients to obtain as critical input their views, experiences, and preferences throughout a product's* lifecycle.*

* It should be noted that participants indicated this definition pertains to all medical-product development. Not just for drugs. Since the objective of the conference was PFDD, the definition offered here is with regard to drug development. However, this definition can be broadened and the words, “medical product” may be substituted for the word “drug” in future discussions.

A proposed Conceptual Framework for PFDD

A conceptual framework for PFDD emerged based upon the meeting discussion and previously proposed models including:

- The National Health Council held a Dialogue on Advancing Meaningful Patient Engagement in Drug Research, Development, and Approval. As part of that work, a framework depicting opportunities for engagement was produced.¹
- The Clinical Trials Transformation Initiative's Patient Groups & Clinical Trials Project prepared a framework depicting patient group assets across the research and development continuum.²
- Perfetto et al. proposed a framework for a patient-focused drug development plan.³

Adapting from these three approaches, the following conceptual framework for patient-focused drug development was constructed. The vision shared by a number of stakeholders at the March M-CERSI meeting was that in the future, biopharmaceutical companies will incorporate patient insights into all stages of drug development, which is divided into the preparation, execution, and communication phases (Figure 3).

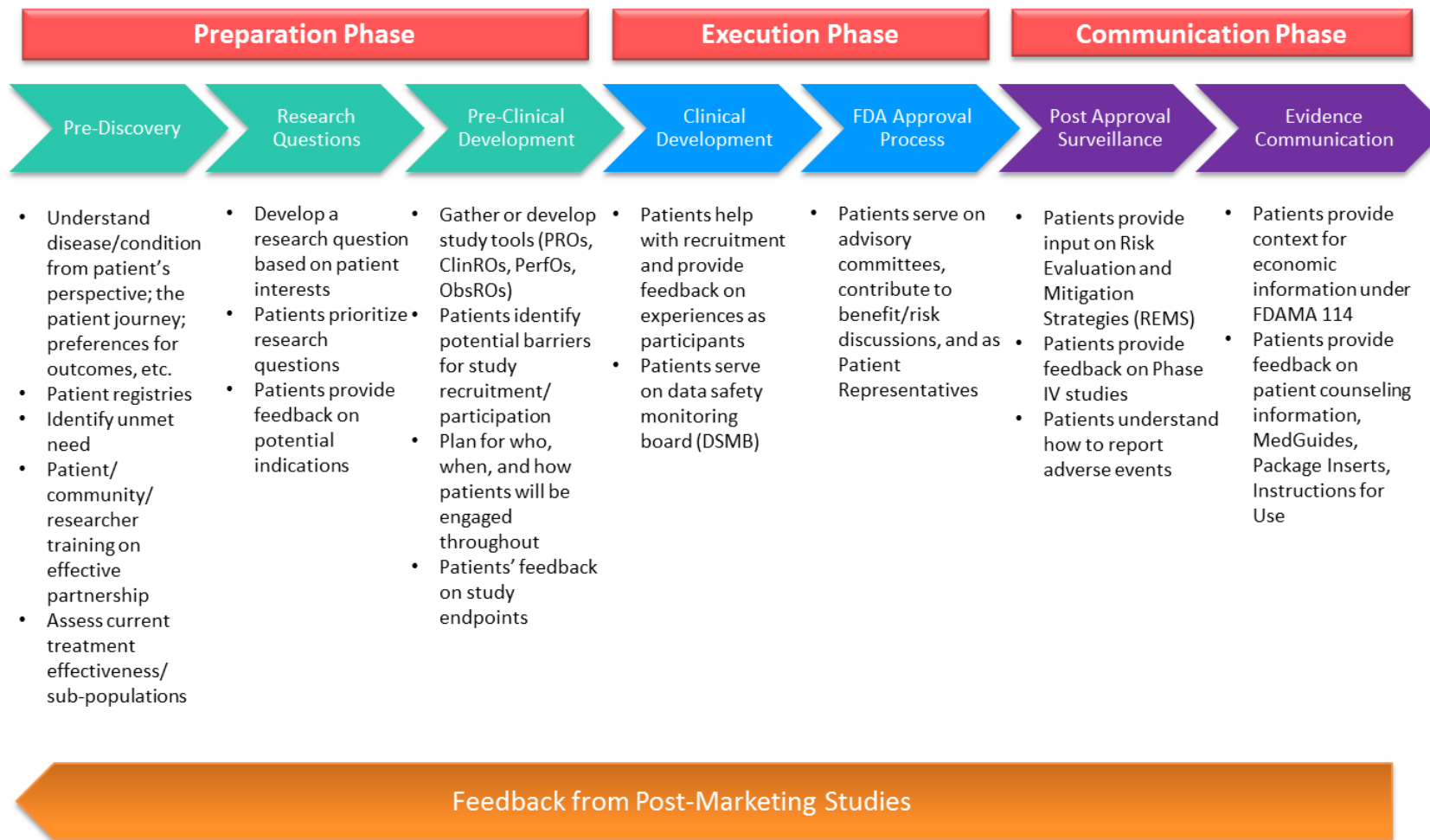


Figure 3. Proposed PFDD Conceptual Framework. Adapted from: Clinical Trials Transformation Initiative's Patient Groups & Clinical Trials Expert Meeting summary; National Health Council's Dialogue/Advancing Meaningful Patient Engagement in Drug Research, Development, and Approval; Perfetto et al Med Care. 2015 Jan;53(1):9-17.

A Proposed Rubric – How do we know the patient has been engaged in drug development?

The meeting discussion captured a range of characteristics that were proposed as to what would constitute sound elements of PFDD. It is difficult for a single or small group of individuals to faithfully represent the patients' perspectives as a whole. The use of science-based methods for gathering patient perspectives ensures that the data collected are valid and representative. The experiences of patients can be heterogeneous and an individual patient's perspective may differ from that of other patients and may change with time as personal circumstances and his or her state of disease or condition changes. It is important that patient participation activities capture the range of and subtleties of patients' perspectives.

These elements were used to formulate the following rubric:

1. Patients as Partners: Patients, caregivers, and other relevant people (e.g., people who are at risk for a disease, but do not yet have the disease) are recognized as partners in the drug development process throughout the life cycle.

Patient Role	Examples	Engagement Level
Partnership role	<ul style="list-style-type: none"> Patients provide a priori and continuous consultation on outcomes of importance, study design, etc. Patients are paid investigators or consultants Patients have a governance role; patients have "a seat at the table" 	High
Advisor role	<ul style="list-style-type: none"> Patients serve as advisory committee members or provide <i>a priori</i> consultation on outcomes of importance and study design, but have no leadership role or governance authority 	Moderate
Reactor	<ul style="list-style-type: none"> Patient input is collected distally through surveys, focus groups or interviews, but patients are not consulted directly or a priori on such things as study design and outcomes of importance Patients are asked to react to what has been put before them rather than being the origin of the concepts of interest 	Low
Study subject	<ul style="list-style-type: none"> Patients are recruited or enrolled as study subjects, but are not asked for input, consultation, or reaction 	None

2. Continuous Patient Engagement: Patient engagement is continuous, throughout the drug development process and product lifecycle; it is not a one-time or sporadic event.

Engagement Continuity	Examples	Engagement Level
Continuous	<ul style="list-style-type: none"> Patients are engaged in various ways throughout all phases of research planning, implementation, analysis, write up, and dissemination stages of the life cycle 	High
Sporadic	<ul style="list-style-type: none"> Patients are asked for input into research planning, study design or outcomes of importance at several points in time but without coordination or meaningful continuity 	Moderate
One-time	<ul style="list-style-type: none"> Patients are only asked for input into research planning, study design or outcomes of importance at one point in time (e.g., early planning or late dissemination) and the study or program proceeds without further patient consultation 	Low
No engagement	<ul style="list-style-type: none"> Patients are not asked for input into such aspects as research planning, study design or outcomes of importance 	None

3. Meaningful Patient Engagement: Patient engagement must be meaningful. That is, it must be a real interaction and dialogue, not a “check-the-box” exercise. Patient input should come from thoughtful dialogue and patients should be able to see how the input they provide is used in the specific studies or in the development processes.

Engagement Meaningfulness	Examples	Engagement Level
Meaningful	<ul style="list-style-type: none"> A plan for interaction and dialogue among stakeholders is outlined with clear objectives, why and how the dialogue will take place, the information sought, how it will be used, and how patients will be kept informed throughout A range of engagement methods can be used as deemed appropriate 	High
Partial	<ul style="list-style-type: none"> Specific activities for meaningful dialogue are 	Moderate

	undertaken but are not comprehensive or well-coordinated <ul style="list-style-type: none"> ● Patient engagement methods are used, but they may not be appropriate or sufficient for the circumstance 	
Superficial	<ul style="list-style-type: none"> ● Informal conversations with patients take place in which their input and views are sought, but there is no interactive dialogue, formal process, or plan for using the information 	Low
No interaction	<ul style="list-style-type: none"> ● No interaction or dialogue is initiated 	None

4. The Right Patients are Engaged: Throughout the process, the target patient population is well represented, and other relevant populations are considered for engagement.

Right Patients	Examples of Engagement	Engagement Level
Comprehensive	<ul style="list-style-type: none"> ● A thoughtful effort is made to engage a range of patients (and caregivers) as is required by the disease and other circumstances (e.g., patients with the disease, cured from the disease, at risk for the disease) ● Patients and patient advocacy groups (large and small) are engaged as per the disease and circumstance ● When possible the range of patients afflicted are represented (e.g., age, gender, race, geography, socioeconomic status) 	High
Representative	<ul style="list-style-type: none"> ● A representative sample of patients is engaged, but may be limited by demographics, region, etc. is not as comprehensive as needed 	Moderate
Limited	<ul style="list-style-type: none"> ● A small number of homogenous patients are engaged ● A “convenience sample” 	Low
No patients	<ul style="list-style-type: none"> ● No patients included 	None

5. The Right Time to Engage: Engagement happens at the appropriate time(s) throughout the process.

Temporality	Examples	Engagement Level
Appropriate	<ul style="list-style-type: none"> ● A clear rationale is provided for the timing of 	High

	<p>patient engagement efforts throughout the life cycle</p> <ul style="list-style-type: none"> • The timing of engagement is well planned based upon the characteristics of the disease/condition, the engagement goals, or other documented rationale 	
Acceptable	<ul style="list-style-type: none"> • A rationale is provided for the timing but is not well supported or does not address all relevant stages of the life cycle 	Moderate
Poor	<ul style="list-style-type: none"> • Unclear rationale and temporality • No clear plan for engagement timing 	Low
Inappropriate	<ul style="list-style-type: none"> • Timing is clearly not appropriate given the disease/condition, study design or for other reasons 	None

Other key discussion points:

Challenges to Successful PFDD:

- The FDA is open to patient advocacy organizations and similar stakeholder groups working collaboratively to lead their own PFDD meetings styled after FDA’s twenty PFDD meetings. However, the FDA has not yet developed formal policy on how “external-led” PFDD meetings might take place.
- The science of patient engagement is still emerging, especially for drug development. Best practices are needed for systematically collecting patient input on their experience of living with a particular disease.
- There is need to identify and test promising patient-engagement methods.
- It is not enough to engage those who are already participating. There is a need to focus on previously missed opportunities to learn from patients and to engage broader patient populations.
- With the help of collaborative partnerships, the Internet and social media information from patients can be captured and used to foster engagement.
- Differences in culture exist and methods for engaging patients may vary internationally.
- A balance has to be attained between the suitability of the engagement method and generation of high-quality evidence.

Patient Advocacy Role

- The role of patient advocacy organizations is expanding including collecting information from the patient community and sharing it with industry and research partners.
- Patients want opportunities to participate in the accelerated approval process.
- Patient advocacy organizations are already collaborating to transition the lessons they have learned through their own PFDD meetings into an operational framework for conducting PFDD programs.

- Patient advocacy groups report that they need to improve harmonization among themselves to avoid duplication and inefficiency in efforts. Aligning efforts and identifying the contributions of advocacy organizations is vital to successful collaboration.

Regulatory Challenges

- Companies face regulatory hurdles, particularly from within their own organization in engaging patients. Many company legal departments approach pre-approval contact with patients conservatively to avoid perceptions of pre-approval promotion.
- As industry aims to solicit guidance from patients on outcomes and preferences, legal and compliance policies can serve as a barrier to meaningful interaction. While these barriers are intended to protect both parties, for companies to meaningfully involve patients. Regulatory guidance is needed for the biopharmaceutical industry to understand how and when they can engage the patient community.

Emerging Payer Role

- Payers are largely underrepresented as stakeholders in “patient-centric” drug development initiatives; in particular, they must be brought into the PFDD dialogue.
- Payers are key decision makers in determining access to biopharmaceuticals and devices for their patient populations. They can contribute to the creation of a unified paradigm or model of patient engagement for continuity between patient engagement in treatment development and patient engagement in healthcare decision making.
- Payer input would be valuable in designing transparent, consistent methodology to ensure that PFDD evidence is useful in real-world decision-making. PFDD can be an avenue to engage patients in the benefit-risk assessment of drugs so payers can better determine how likely their patient population will tolerate, and therefore be more willing to use, a specific treatment.

Future Directions and Opportunities for Collaboration

- All stakeholders (patient community, industry, academic researchers, government, health systems, providers, and payers) must collaborate.
- Methods development is critical to improve the capture of the right information from the right patient populations at the right time in efficient and valid ways and to improve the use of that information in development programs and benefit-risk assessment.
- Tangible incentives, both regulatory and market-based, are needed so that patients, payers, and biopharmaceutical companies benefit from this transformative initiative.

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Appendix A. M-CERSI Conference on PFDD

Table 1. M-CERSI Conference on PFDD Planning Committee Members

Organization	Committee Member(s)
AstraZeneca	Kathy Gans-Brangs, Ph.D
Avalere Health	Tanisha Carino, Ph.D
CEOi	Drew Holzapfel
Critical Path Institute	Stephen Joel Coons, Ph.D
Epstein Health	Robert Epstein, MD, MS
FDA	Theresa Mullin Ph.D., Ashley Slagle, M.S., Ph.D, Sara Eggers, Ph.D, Pujita Vaidya, M.P.H.
Kaiser Permanente	Murray Ross, Ph.D
Lora Group	Laurie Burke, R.Ph., M.P.H.
M-CERSI	James Polli, Ph.D, R.Ph. and Ann Anonsen
Merck	Jeanne Regnante, MS
National Health Council	Marc Boutin, JD
National Organization for Rare Disorders	Peter Saltonstall
National PKU Alliance	Christine Brown, M.S.
National Quality Forum	Karen Johnson, M.S., Ph.D.(c)
Novartis	Gretchen Trout
PatientsLikeMe	Sally Okun, BSN, R.N., MMHS
Parent Project Muscular Dystrophy	Pat Furlong
Pfizer	Roslyn Schneider, M.D., MSc
PhRMA	Kristin Van Goor, PhD
PROEM	Eleanor Perfetto, Ph.D., M.S., Elisabeth Oehrlein, and Chinenye Anyanwu, Pharm.D., MPH
Sanofi	Anne Beal, M.D., M.P.H.

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www.pharmacy.umaryland.edu/patient_focused_drug_development