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M-CERSI CONFERENCE ON PATIENT-FOCUSED DRUG DEVELOPMENT

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.

Stakeholder Perspectives on Patient-Focused Drug Development:
Insights from FDA, Patients, Industry, and Payers

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Table of Contents

| | |
|--|-----|
| Abstract | 1 |
| Executive Summary | 3 |
| Session 1: FDA Activities in and Goals for PFDD..... | 6 |
| Session 2: Patient Activities, Challenges, and Aspirations | 9 |
| Session 3: Current Industry Activities and Plans..... | 12 |
| Payers: Why They Should Join the Dialogue | 14 |
| Future Directions and Opportunities for Collaboration..... | 15 |
| Conclusions | 16 |
| Definition for PFDD..... | 18 |
| A Proposed Rubric – How do we know the patient has been engaged in drug development?..... | 21 |
| References | 26 |
| Appendix A. M-CERSI Conference on PFDD..... | I |
| Appendix B. Example PFDD Meeting..... | III |

Abstract

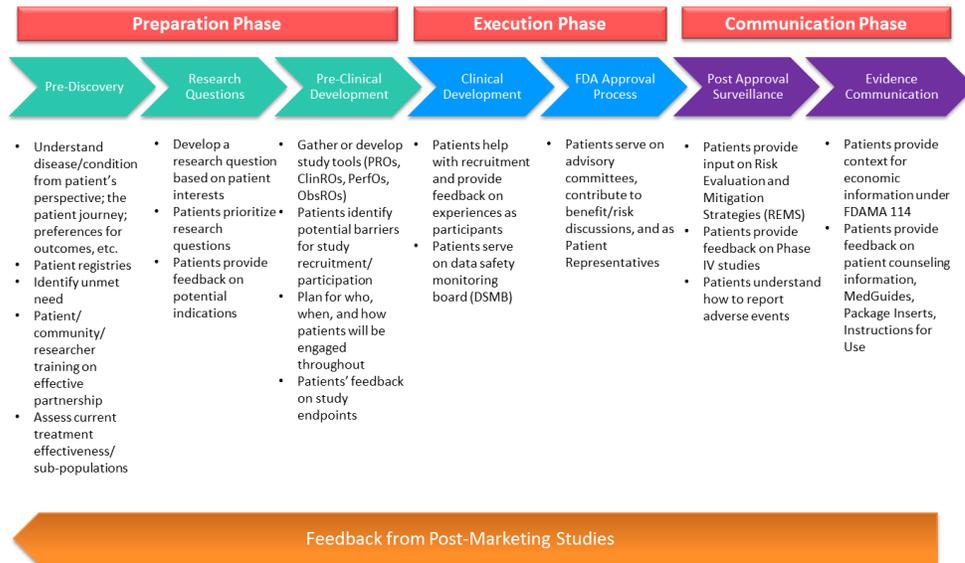
A movement to include the patient voice in health care research and decision making is underway. In light of broad stakeholder interest in patient-focused drug development (PFDD), a range of stakeholders are considering approaches to increase the scope of PFDD and enhancing patient engagement. On March 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 stakeholders’ perspectives on and understanding of the definition and attributes of PFDD as well as its potential for achieving the goal of including the patient’s voice in drug development. The role of various stakeholders and opportunities for their active participation were outlined. The outputs of the conference included a suggested definition, rubric, and framework for PFDD:

Definition: *Patient-focused drug development is a formal process by which drug* developers and regulators form a partnership with patients 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.*

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 product life cycle.
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.
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 aspects of processes.
4. The Right Patients are Engaged: Throughout the process, the affected patient population is well represented, and other relevant populations are considered for engagement.
5. Right Time to Engage: Engagement happens at the appropriate time(s) throughout the process.

Conceptual Framework: Building upon previously proposed models and the meeting discussion, a conceptual framework for PFDD emerged.



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; and the model proposed by Perfetto et al. Med Care. 2015 Jan;53(1):9-17.

Executive Summary

In the United States and Europe, a movement to include the patient voice in health care research and decision making is underway. More recently, patient centeredness is being incorporated into medical product development, particularly for drugs and medical devices. For example, patient-focused drug development (PFDD) is part of an ongoing initiative by the Food and Drug Administration (FDA) to incorporate the “patient voice” in drug development. In light of wide stakeholder interest in PFDD and based on FDA learnings from the first several years of its 5-year PFDD initiative, the FDA and other stakeholders are considering approaches to increase the scope of PFDD and enhance 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 the FDA, patient groups, the biopharmaceutical industry, payer and other organizations to voice their views on, activities in, and aspirations for PFDD. This document summarizes stakeholders’ perspectives on and understanding of the definition and attributes of PFDD as well as its potential for achieving the goal of including the patient voice in drug development. The role of various stakeholders and opportunities for their active participation are outlined. The outputs of the conference included a suggested definition, rubric, and framework for PFDD.

A Definition of 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. In the minds of most stakeholders, the scope of PFDD extends beyond the public “voice-of-the-patient” meetings currently being conducted by the FDA, to developing rigorous methods for patient engagement and systematic data collection throughout a product lifecycle. PFDD has been discussed as a process by which we bring new medicines to people, informed throughout the path by input from persons living or trying to prevent 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. PFDD extends beyond drugs to all treatments and diagnostics.

A recommended definition was developed based on the discussion:

Patient-focused drug development is a formal process by which drug developers and regulators form a partnership with patients 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.*

A Proposed Conceptual Framework for PFDD

Building upon previously proposed models and the meeting discussion, a conceptual framework for PFDD emerged.

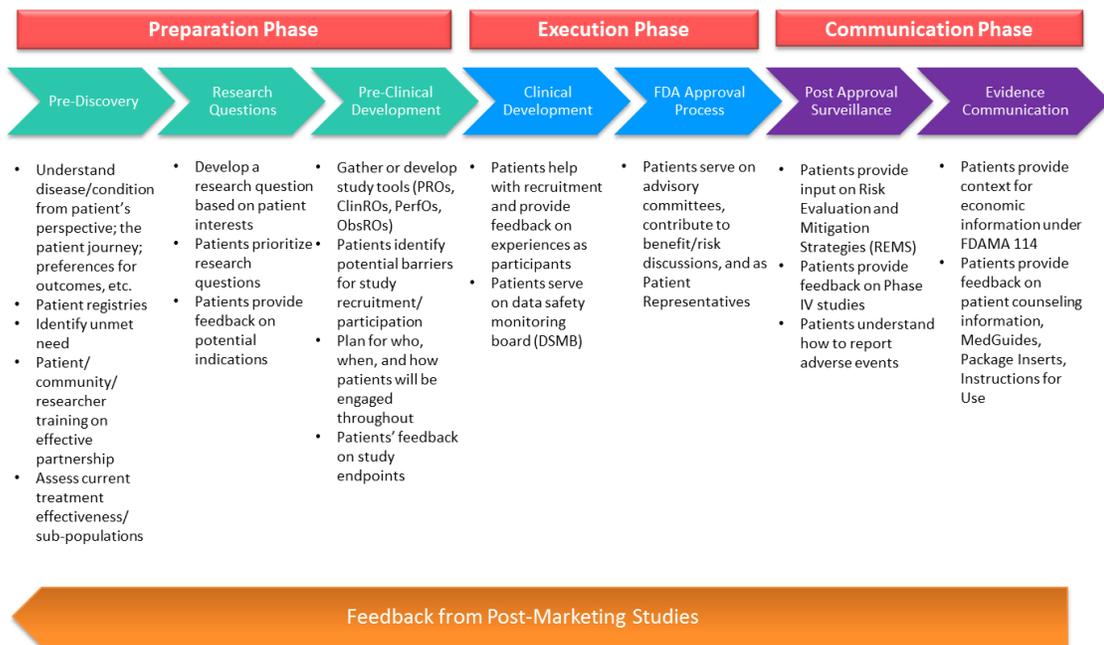


Figure: Proposed PFDD Conceptual Framework. Adapted from: Clinical Trials Transformation Initiative's Patient Groups & Clinical Trials Expert Meeting summary; National Health Council's Dialogue/Advancing Meaningful Patient Engagement in Drug Research, Development, and Approval; and the model proposed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

* 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 to discuss 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.

Stakeholder Perspectives on Patient-Focused Drug Development: Insights from FDA, Patients, Industry, and Payers

Background

In the United States and Europe, a movement to include the patient voice in health care research and decision making is currently underway. In the United States, this growing interest is perhaps best exemplified by the Patient-Centered Outcomes Research Institute (PCORI), established under the Patient Protection and Affordable Care Act (ACA) and a primary funding source for patient centered outcomes research (PCOR). PCOR seeks to aid individuals and their caregivers to “communicate and make informed healthcare decisions” by requiring researchers and patients to work together to formulate and complete studies.¹ In Europe, patient-identified priorities have also become increasingly prominent in health technology assessment (HTA) for medical products. Regional HTA bodies, such as the UK’s National Institute for Health and Care Excellence (NICE) and Germany’s Institute for Quality and Efficiency in Health Care (IQWiG), are increasingly engaging patients directly in review or in pilot projects to determine how patients can best contribute to decision-making.^{2,3,4,5}

Other efforts such as emphasis on community-based participatory research and shared decision-making in medical care also contribute to growing “patient centeredness” focus in healthcare. As depicted in Figure 1, there is an emphasis on understanding the patient experience, sometimes referred to as the patient journey. This most often includes capturing information from those with the disease but can also include caregivers and family members. Their views about their condition, experiences, goals, and preferences are a critical part of research and also a critical part of shared decision making in their own care. The figure depicts the flow of patient experience data into these two critical, overlapping paths.

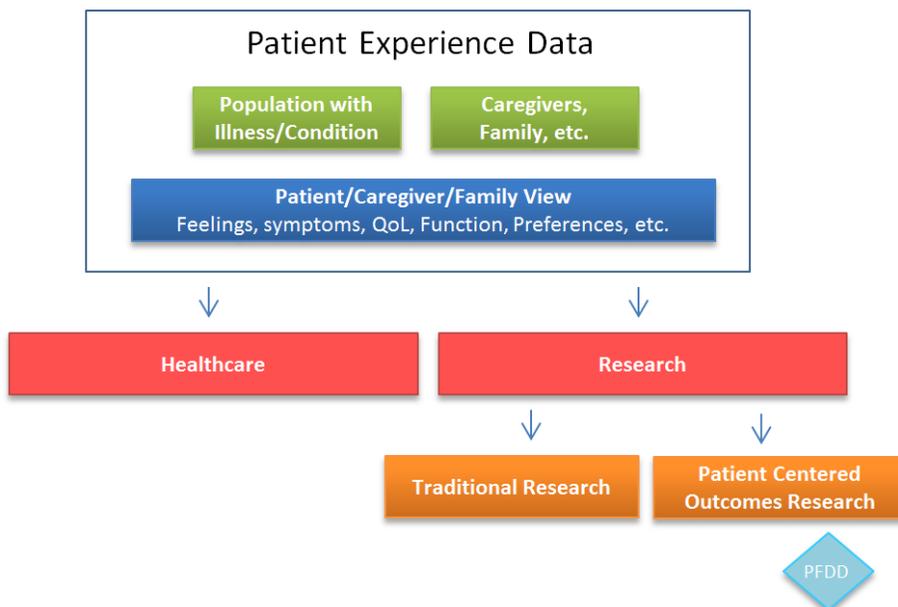


Figure 1. Patient-Centeredness in Healthcare; PFDD= Patient-Focused Drug Development, QoL=quality of life

More recently, patient centeredness is being incorporated into medical product development. For example, patient-focused drug development (PFDD) is part of a five-year initiative conducted by the Food and Drug Administration (FDA) to more systematically obtain the patient perspective on certain diseases and their treatments.⁶ PFDD research is one branch of PCOR as patient input is used in PCOR in many ways in the drug development process (Figure 1). Biopharmaceutical companies and patient advocacy groups have been very supportive of this initiative and are contributing to it by working toward more widespread incorporation of patient input into the process.^{7,8} Both the Pharmaceutical Research and Manufacturers of America (PhRMA) and the National Health Council (NHC) have identified PFDD as a top priority for the next reauthorization of the Prescription Drug User Fee Act (PDUFA VI), as well as for the 21st Century Cures legislation, indicating that early stakeholder engagement will become increasingly important for successful drug development.

In light of wide stakeholder interest in PFDD and based on FDA learnings from the first several years of its 5-year PFDD initiative, the FDA and other stakeholders are considering approaches to increase the scope of PFDD and enhancing patient engagement.⁹ For example, the Clinical Trials Transformation Initiative (CTTI) was pursuing a project to identify how and when interaction with patients is most useful during clinical trials. Its work is now publicly available.¹⁰ Separately, the National Health Council has produced a report on “*Advancing Meaningful Patient Engagement in Drug Research, Development, and Approval*,” which was a multi-stakeholder effort.¹¹

As with any new, cutting-edge program, stakeholders have many questions about PFDD and are eager to understand their roles, as well as the initiative’s benefits and foreseeable challenges. 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 (Appendix A), held the “M-CERSI Conference on PFDD.” These proceedings summarize the M-CERSI PFDD Conference presentations and discussions. The objective was to allow stakeholders from the FDA, patient groups, the biopharmaceutical industry, payer and other organizations to voice their views on, activities in, and aspirations for PFDD. This document summarizes stakeholders’ perspectives on and understanding of the definition and attributes of PFDD as well as its potential for achieving the goal of including the patient voice in drug development. It also discusses the perceived role of stakeholders and opportunities for their active participation. These proceedings conclude with a discussion on future opportunities and challenges for PFDD while providing suggested next steps. The outputs of the conference included a suggested definition, rubric, and framework for PFDD.

Session 1: FDA Activities in and Goals for PFDD

In this first session, the FDA staff highlighted three FDA programs related to engaging patients in the drug development and review process. FDA staff reviewed FDA’s vision

for PFDD, along with additional FDA programs promoting patient centeredness in medical product development.

FDA's Patient-Focused Drug Development Initiative

The FDA PFDD initiative, spearheaded by **Theresa Mullin, PhD, Director, Office of Strategic Programs**, is largely facilitated by FDA's Office of Strategic Programs (OSP) in the Center for Drug Evaluation and Research (CDER).

"Patients know and feel what would make a difference to them and their lives." Dr. Theresa Mullin 2015

Dr. Mullin reported that FDA PFDD meetings completed to date demonstrate that patients are very interested in having their voices and insights documented and acted upon by relevant stakeholders (See Appendix B for sample meeting questions). Given the diversity of the patient population in the United States and number of diseases for which products are in development, it is well recognized that the FDA does not have the resources to facilitate a PFDD patient-engagement meeting for all possible disease areas. Dr. Mullin presented on the opportunity for externally-led patient-focused drug development meetings, welcoming patient organizations to identify and organize patient-focused collaborations to generate public input on other disease areas, using the process established through Patient-Focused Drug Development as a model. Like FDA's PFDD meetings, externally-led meeting could provide a platform for patients and their caregivers to contribute to the facilitated dialogue. Patients groups could explore different mechanisms to organize and host these meetings, e.g., public meetings, web-only meetings, and other possible mechanisms to collect public input. Patient groups considering organizing their own externally-led, PFDD meeting, are recommended to submit a letter of intent, informing the FDA of the meeting while stating the importance of the event and including a draft agenda. The information provided to the FDA will enable them to be actively involved and notify other relevant stakeholders about the PFDD meeting. Current information (as of November 2, 2015) on the opportunity to conduct externally-led Patient-Focused Drug Development meetings can be found online.¹²

Dr. Mullin concluded her presentation with a discussion on the potential broader opportunities to bridge from FDA's PFDD initiative and advance the science of patient input into drug development. She noted, for example, the value in engaging a wider community of patient stakeholders, clinicians and social science researchers to identify methodologically-sound approaches for systematically collecting patient input on their experience of living with a particular disease and for incorporating this into the benefit risk assessment and potentially product labeling.

The Role of Patients in Health Outcomes Assessment: A Regulatory Perspective

Dr. Ashley Slagle PhD, Clinical Outcome Assessment Staff (formerly known as Study Endpoint and Labeling Development), FDA, provided background on one of the most visible, existing means of incorporating patient input into drug development: the use of clinical outcome assessments (COA), including patient-reported outcomes (PROs), in clinical trials. The purpose of an outcome assessment is to “determine whether or not a drug has been shown to provide benefit to patients.” One of the most important aspects of drug development is how treatment benefit is measured. Clinical outcome assessments should be well-defined and reliable, and measure aspects of health and treatment that represent something meaningful to patients.

Qualitative research (e.g., focus groups, patient interviews) can be used to develop or select meaningful and appropriate clinical outcome assessments for use in clinical trials. The FDA PRO Guidance describes good measurement principles to consider when developing or selecting well-defined and reliable patient reported outcome assessments, and provides recommendations about how to incorporate patient input into this process.^{13,14} This guidance provides an optimal approach to this, though FDA understands that flexibility and judgment are needed in order to meet both regulatory standards as well as the practical demands of drug development.

While PROs are often considered for inclusion in trials, there are other types of COAs that can provide meaningful information to patients that should be considered when a self-report might not be feasible within a clinical trial. Other COA types include performance outcomes (PerfOs), clinician-reported outcomes (ClinROs), or observer-reported outcomes (ObsROs). Dr. Slagle described the “FDA Roadmap to Patient-Focused Outcome Measurement in Clinical Trials,” and explained that this is not a requirement, but “illustrates how one might embark upon a sound, orderly, instrument selection or development pathway for clinical outcome assessment”, beginning with understanding the disease or condition, and conceptualizing treatment benefit.¹⁴ Patient input into each of these elements is valuable and important.

When asked how much overlap there is between traditional expert opinion and new information from patients, Dr. Slagle stated that sometimes a “substantial gap” exists between the insights provided by patients and clinicians, and that while clinical experts also provide important information, they cannot provide all of the important insights that patients living with a condition are able to provide.

FDA Patient Representative Program

Richard Klein, Director, Patient Liaison Program, FDA Office of Health and Constituent Affairs, described a long-established collaboration between patients and the FDA: the Patient Representative Program. This program, established in 1991, organizes opportunities for patient representatives to sit on FDA Advisory Committees. To become a “Patient Representative,” an individual must have: (1) personal experience with the disease or condition as either a patient or primary caregiver; (2) be both active in relevant patient advocacy activities and knowledgeable of treatment options and ongoing research; (3) have experience with decision-making based on complex

information and be “analytical and objective” and (4) have minimal or no conflicts of interest. The program currently involves approximately 200 Patient Representatives representing 120 diseases/conditions.^{15,16} These patients provide important insights from the patient perspective.

Mr. Klein provided one example of a patient’s contribution: *“As I listened, I heard the entire conversation focusing on a quick, 15-minute, in-office ‘snip-and-stitch’ procedure, ‘nothing to it’... I commented that there was far more to ‘the procedure’ than the surgeons’ clinical assessment, and that as a patient having had so much very painful vaginal surgery, I could attest to the fact that this ‘snip-and-stitch’ might be 15 little minutes of their time, but, for the patient, it could mean two to three weeks of misery while the incision and stitches healed.” –Barbara, OB/GYN*

Mr. Klein also described a new program, the Patient Consultant Program, initiated to fulfill obligations under Section 1137 of the FDA Safety and Innovation Act (FDASIA). This program aims to incorporate “patient participation in medical product discussions.” Patient consultants work directly with FDA scientific review staff and may participate in sponsor meetings with the agency.^{15,16}

Finally, Mr. Klein also discussed the FDA Patient Network, which broadens opportunities for patient engagement through webinars, in-person meetings, and a bi-weekly newsletter providing information on new product approvals, labeling changes, safety warnings, and other important information.^{15,16}

Session 2: Patient Activities, Challenges, and Aspirations

The session on patient activities was opened by **Pat Furlong, Founding President and CEO of Parent Project Muscular Dystrophy (PPMD)** who described how 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. For example, PPMD conducted its own “external-led” PFDD meeting and submitted draft guidance for drug development in Duchenne Muscular Dystrophy to the FDA.¹⁷ PPMD’s experience can serve as a roadmap for other groups interested in conducting their own PFDD meetings.

Ms. Furlong stressed one area that patient advocacy groups believe they need to improve upon is harmonization among the groups to avoid duplication and inefficiency in their efforts. For example, there are multiple Duchenne advocacy organizations, but there will be only one FDA guidance on drug development in Duchenne. Aligning efforts and identifying contributions for each of the advocacy organizations will be vital to successful collaboration.

Advancing Meaningful Patient Engagement in Drug Research, Development, and Approval

Marc Boutin, CEO, National Health Council stated that, in his view, PFDD will make the healthcare system more cost effective, largely by creating treatments that are of high value to patients. “What is exciting is that we are seeing the drug and biopharmaceutical industry move in this way, which will give us high value products that will move into the delivery system. If you bring these products into a delivery system that is equipped to actually identify a patient’s preference and match those products to those individual patients, what you do is eliminate all the [unnecessary] care, which is produced in trial and error. And as a result, you can eliminate a lot of waste that is in the system and actually bring health care costs down.”

According to Mr. Boutin, there is currently no widely accepted, cross-stakeholder definition of PFDD. Establishing consensus on a definition will be vital in moving forward with the initiative. The next steps will include: (1) identifying promising patient engagement methods; (2) defining meaningful patient engagement; and (3) identifying barriers to meaningful engagement and solutions for those barriers. In order to move forward in advancing patient engagement, all stakeholders (patient community, industry, academic researchers, government, health systems, providers, and payers) must collaborate. To avoid potential barriers to meaningful patient engagement, Mr. Boutin identified key themes for identifying meaningful solutions (Table 1).⁸

Table 1: Key Themes for Overcoming Barriers to Meaningful PFDD

| Key Themes for Potential Solutions |
|--|
| Clear signals and transparency from all stakeholders |
| Regulatory action to set guard rails |
| Methods and tools for systematically engaging patients |
| Communication tactics targeted to patients |
| Coordinated and strategic dissemination efforts |
| Infrastructure for sharing best practices |
| Organizational culture shifts at all levels |
| Systemic changes to incentivize patient engagement |

Patient-First Drug Development: Exploring the Patient Perspective

“PFDD needs to be converted from an object of wonder to regular day-to-day procedure through collaborative accomplishment.” Sally Okun, RN, PatientsLikeMe, 2015

Sally Okun, RN, Vice President, Advocacy, Policy and Patient Safety, PatientsLikeMe, stated that “Patient-focused drug development has been really something that we have been talking about in different pockets and different circles for a long time.” From our perspective at PatientsLikeMe, “being sure that we are putting patients first is really the key piece of this; that we have to constantly be finding ways of

engaging as many as possible across as diverse a population as possible. That will ultimately bring PFDD into the 21st century in a way that FDA can embrace and enjoy the opportunity to work with groups that previously have been a little more difficult for them to reach.” It is not enough to engage those who are already participating in clinical trials or other research, there is a need to focus on acknowledging previously missed opportunities to learn from patients, and to engage the broader patient population.

A balance has to be attained between suitability of the method and generation of high-quality evidence. One is to connect narratives from a wide variety of patients through condition-specific advocacy groups or via web platforms. For example, PatientsLikeMe recently conducted a study among 6,800 randomly selected members with prior clinical trial experience. The objective was to understand motivations, barriers, and opportunities to enhance clinical trial recruitment for patients with chronic illness through a patient-powered research network. Twenty-four percent (n=1,621) of the randomly selected group completed the survey. Their responses illuminated roadblocks and missed opportunities for patient participation in research. The most important factors considered in participation in research included: (1) opportunity to improve own health; (2) medical bills covered if injured; (3) reputation of researchers. Among the least important factors are (1) being paid to participate; (2) possibility of placebo; (3) number of visits and time to participate.¹⁸

Tom Murphy, BS, is a patient with amyotrophic lateral sclerosis (ALS) and has been a PatientsLikeMe member since his diagnosis in 2010. He stated that for patients, the “majority of disease information comes from the patient and not the healthcare community.” Through the internet and social media, patients are more informed about drug treatments and procedures than ever before. With the help of collaborative partnerships, this information should be captured and used to foster drug development and better availability of effective drugs that meet the needs of the American public.

Mr. Murphy stated, “The best way to move forward with PFDD is to come up with innovative ways to involve large numbers of patient populations from diverse disease communities to get involved in the drug development-related processes.” Patients want opportunities to participate in study design and the accelerated approval process, since they have a vested interest in the process moving along as quickly as possible.

Sally and Tom’s recommendation on the “Etiquette of Engagement”

“Listen frequently, take the time to know that you have heard patients, invite patients, act respectfully, ask meaningfully, share, collaborate, and measure rigorously. Learn while you listen carefully.”

Patient Focused Drug Development: The Journey of the National PKU Alliance

“Patient advocacy groups now want to go beyond collecting funds for research and look for opportunities to get involved in or influence accelerated drug development.” Christine Brown, 2015

Christine Brown, MS, Executive Director, National PKU Alliance (NPKUA)

increasingly sees the role of the organization she leads as one of collecting information from the community and sharing it with industry and researcher partners. Under Ms. Brown's leadership, NPKUA has gone beyond providing funding to researchers, to being an active participant in development of next generation therapies. For example, by facilitating web-based surveys, patient advocacy groups like the NPKUA learn about currently available treatments, which risks are acceptable to patients, and which symptoms and lifestyle factors are most important to patients. Beyond facilitating information from patients, NPKUA is also conducting interviews of other key stakeholders for the condition, for example, they conducted key informant interviews with leading medical professionals to gain a comprehensive understanding of their views.¹⁹

Another successful approach in sharing the patient voice with researchers implemented by NPKUA was holding a patient conference in conjunction with an International Scientific Exchange. The organizers found that each of the researcher participants stayed to listen to the patients, ensuring the patient voice was heard.

Session 3: Current Industry Activities and Plans

Pharma's Role in Getting Patients Ready to Partner in Development

"One challenge is understanding and being able to manage the regulatory environment. So clearly, there is a lot of regulation in this industry, a lot of rules in terms of what we can and cannot do, and can and cannot say." Anne Beal, 2015

The pharmaceutical industry acknowledges that PFDD begins with the patients' journey and involves understanding what it means to live with a disease. **Anne Beal, MD, MPH, Chief Patient Officer, Sanofi**, pointed out that understanding both are fundamental components of drug development. In recent years, industry has become very receptive to the PFDD initiative. Conversations have shifted from, "Why should patients be involved in drug development?" to "How do we ensure patients are at the core or center of the drug development process?" this is indicative of the value of the patients' voice and a culture shift within the industry. For PFDD to be truly "patient-centric," patient engagement needs to be a planned component of the process and should, not occur only at the point when help is needed for clinical trial enrollment or retention.²⁰

Core values for patient centeredness should be: transparency, partnership, continuous learning and improvement, and a focus on outcomes and impact. While *"patients want to be engaged, researchers want to engage, and there is a lot of interest in really making sure the patients voice is heard"* there are certain challenges that may stand in the way of effective collaboration. These challenges include patient readiness, research(er) readiness, cultural variation, and the legal/compliance environment.

There are currently a number of groups involved with improving "patient readiness." For example, the European Patients' Academy on Therapeutic Innovation" (EUPATI), patient

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universities, and Academy Health. PCORI has taken the lead on “researcher readiness” through documents such as the Patient Engagement Rubric.²¹

As industry aims to solicit guidance from patients on clinical outcomes and patient preferences, legal and compliance policies sometimes serve as a barrier to meaningful interaction. While these barriers are intended to protect both parties, in order for drug manufacturers to meaningfully involve patients, mechanisms must be developed to enable appropriate communication. According to Dr. Beal, certain challenges still exist in the legal/compliance space, especially when attempting to gain insights from patients around the world. For example, significant variations exist in terms of rules regarding patient engagement, but differences in culture also exist. American methods of engaging patients may not work internationally. To move forward, patient protection must be balanced with access to patients.²⁰

Patient-centricity: Making Stone Soup

“Patient centricity is like stone soup. We are starting at the beginning even before the clinical trials with the broth of our targeted concepts. We add ingredients, which are the relationships, resources, and functional expertise of many, and as the soup simmers we try to ensure good patient outcomes.” Roslyn Schneider, 2015

According to **Dr. Roslyn Schneider, MD, MSc, Global Patient Affairs, Pfizer**, in order to move patient-centricity to the next horizon, across health-related organizations we should move from listening and understanding the patient journey to “strategic integration of the patient experience.” This would mean an alignment of priorities, engagement and inclusion in development, and exchange of relevant, understandable information. To facilitate the systematic inclusion of patient insights, two questions should be asked repeatedly: “Did we ask patients?” and “Did we change anything after their input?”²²

Pfizer has implemented several online programs to make information about participating in and understanding clinical trials more accessible to patients. *Pfizer Link* is a type of “alumni association” for participants of Pfizer clinical trials to obtain information on study results and share their experiences of participating in clinical trials. The evolving website contains lay-language clinical summaries, insights from patients, study results from Pfizer clinical trials, and invitations to participate in other relevant research.²³

In addition, Pfizer has created a website, *Pfizer Patient-Reported Outcomes*, which contains information on measures developed by Pfizer for a variety of therapeutic areas. These measures, which include those designed for use in clinical research for clinical outcomes assessment and screening are available free of charge to academic researchers and individual clinical practices.²⁴

Another means that Pfizer has developed for making patient-accessible health information widely available is the GetHealthyStayHealthy website.²⁵

To improve patient access to information, a collaboration in the US among Eli Lilly, Pfizer, and Novartis has also established the, “Patients to Trials Consortium,” which is designed to enable patients to find, understand, and “match” to clinical studies meeting their needs.²⁶

Patient Focused Drug Development: The Time is Now

“Patient-focused drug development is a process by which we bring new medicines to market, informed by input from persons living with diseases at every step of the path, including beyond development and approval to market access. We need to understand from the patients’ perspective what is of value to them, what is the unmet medical need, and what do we need to build in to determine what our products do to make their lives better.” Marjorie Gaitlin, 2015²⁷

“Patient engagement is a mindset and a framework, it goes way beyond just the regulatory process,” **Marjorie Gatlin, MD, VP and Head of Patient and Specialty Services, Novartis**, told the group. She stated that patient engagement cannot end with product approval, but that patients also play a key role in ensuring access, defining value, and informing disease management and adherence programs. Companies must meet the challenges of PFDD as she outlined in Table 2.

Table 2. Meeting the Challenges of Direct Patient Engagement

| Is your company ready for direct patient engagement? |
|---|
| <ul style="list-style-type: none"> ● Build cross-functional consensus on the urgency for direct engagement |
| <ul style="list-style-type: none"> ● Define frameworks and put processes in place to engage patients throughout the lifecycle of a product |
| <ul style="list-style-type: none"> ● Ensure that you have alignment with your patient advocacy department |
| <ul style="list-style-type: none"> ● Create processes for setting up appropriate consulting agreements and contracts |
| <ul style="list-style-type: none"> ● Determine how insights will be archived and shared across the organization |
| Who is the right patient? |
| How do you ensure that you have heard all relevant patient perspectives? |
| How do you reach the patients? |
| <ul style="list-style-type: none"> ● Patient advocacy groups |
| <ul style="list-style-type: none"> ● Clinical trial investigators |
| <ul style="list-style-type: none"> ● Leverage technology (social media, online communities, etc.) |

Payers: Why They Should Join the Dialogue

The PFDD process does not end after a drug receives regulatory approval; patients and stakeholders need to be engaged throughout the entire life cycle of the product. Payers are key decision makers in determining access to biopharmaceuticals for their patient population. They can contribute to the creation of a unified paradigm or model of patient

engagement to determine at where PFDD would be useful in the drug development process. Specifically, payer input would be valuable in designing transparent, consistent methodology to ensure that PFDD evidence will be useful in real-world decision-making. For example, payers often find it difficult to assess “real world tolerability” of pharmaceuticals. PFDD can be an avenue to engage patients in the benefit-risk assessment of drugs so that payers can better determine how likely their patient population will tolerate, and therefore be more willing to use, a specific product.

Dr. Murray Ross, Vice President, Kaiser Foundation Health Plan, Inc. and Director, Kaiser Permanente Institute for Health Policy, discussed opportunities and challenges to moving PFDD forward with PFDD from the managed care perspective. These include methods to quantify tolerance of risk, balancing benefit and risk, operationalizing electronic medical records in such a way that patient preferences can become a mirror image of prescribing patterns, payment and reimbursement, and ultimately the PFDD process.

The final discussion panel pointed out that payers represent an avenue for ensuring that industry is meaningfully engaged in the PFDD process. Providing companies, payers, and patients with the opportunity to interact could yield significant benefits for patients. This collaboration will ensure that the evidence generated will benefit all: payers will have access to information that will directly impact their ability to provide quality care to their beneficiaries (e.g., information regarding heterogeneity of treatment effects in certain subgroups), companies will have evidence that their product has value to patients and payers, and patients will have access to drug treatment options that address health care questions relevant to their needs and aspirations.

Future Directions and Opportunities for Collaboration

Table 3. Ten gaps and Needs Areas for PFDD. (Adapted from comments by Dr. Robert Epstein)

| | | |
|---|----------------------------------|---|
| 1 | Timing of Patient Input | Exactly when would patient input matter? Why would it matter at these points? |
| 2 | Type of Patient Input | How do we utilize quantitative input when thinking about heterogeneity of patient populations? |
| 3 | Sampling | How do we develop unique and innovative ways to engage large numbers of patients? |
| 4 | Endpoints | Do patients really care about patient-reported outcomes? Are they relevant? |
| 5 | Co-Morbidities | People typically have more than one health problem. How do we incorporate that aspect directly into clinical development? |
| 6 | Addressing Other Patient Metrics | How do you integrate benefit / risk assessment from the patient perspective? How do you take into account patient preferences? How do we address gaps in data collection? |
| 7 | Chief Complaints are Ignored | If patients visit their provider with a chief complaint, why aren't we doing something with this information? |
| 8 | Redefining the | How should we redefine the question in the patient's voice? What is |

| | Research Question | the research question that a patient would ask? |
|----|-------------------------|--|
| 9 | Uncertainty Measurement | How will reducing patients' uncertainty better help to reduce the standard deviation and help us get the signal out of the noise? |
| 10 | Myth Breaking | How do we eliminate confusion around FDA legal and compliance barriers slowing down stakeholders trying to get into this conversation? |

Conclusions

PFDD is currently in its early stages. Current and future challenges include establishing tangible incentives, both regulatory and market-based, so that patients, payers, as well as biopharmaceutical manufacturers benefit from this transformative initiative.

Currently, PFDD – in name – is viewed by some as being limited to activities sponsored by the FDA. However, patient engagement in the development of biopharmaceuticals is rapidly expanding. According to Marc Boutin, Chief Executive Officer, National Health Council, “We have been pushing patient engagement as part of PDUFA and PCORI” and looking at a patient-centric agenda, not only in drug development process, but also in the regulatory review process and access to evidence-based care. FDA plays a pivotal role in PFDD, but FDA represents only one stakeholder. While drug development can take up to 8 to 15 years, the product is only with the FDA for review for a short period of time. There is quite a lot of patient engagement that has to happen before the *patient-focused* product gets to the FDA for review. Hopefully, in the near future, this platform will expand to provide opportunities for collaboration between payers and manufacturers to elicit mutual target areas for development. This will guide manufacturers to develop biopharmaceutical products that are valuable not only to patients, but also to payers, so as to ensure the innovation has the potential for coverage and payment.” As Mr. Boutin noted, “to advance patient engagement, we all have to come together and we have to figure out how to do this in an interdependent way. It’s only going to work with partnerships. No one stakeholder can do it all.”

In the minds of most stakeholders, the scope of PFDD extends beyond the public voice-of-the-patient meetings currently being conducted by the FDA, to developing rigorous methods for patient engagement and systematic data collection throughout a product lifecycle. In addition, regulatory guidance is needed for the biopharmaceutical industry to understand how and when they can engage the patient community. Lastly, at present, payers are largely underrepresented as stakeholders in “patient-centric” initiatives; in particular, they must be brought into the PFDD dialogue.

Deliverables from this Conference:

In addition to this proceedings document, there were three planned deliverables for the conference stemming from the discussion: a proposed definition of PFDD, a conceptual framework, and a proposed rubric for PFDD. These are described below:

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. ¹¹ As part of that work, a framework depicting opportunities for engagement was produced.
- The Clinical Trials Transformation Initiative's Patient Groups & Clinical Trials Project prepared a framework depicting patient group assets across the research and development continuum. ¹⁰
- Perfetto et al. proposed a framework for a patient-focused drug development plan. ²⁸

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 |

| | | |
|----------------|--|------|
| | <ul style="list-style-type: none"> undertaken but are not comprehensive or well-coordinated ● 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.

References

1. PCORI. Patient-centered outcomes research. <http://www.pcori.org/research-results/patient-centered-outcomes-research>. Accessed 9/2/2015.
2. Analytic hierarchy process (AHP) - pilot project to elicit patient preferences in the indication "depression". Institute for Quality and Efficiency in Health Care Web site. https://www.iqwig.de/download/Executive-summary-of-working-paper_Analytic-Hierarchy-Process-pilot-project.pdf.
3. Choice-based conjoint analysis: Pilot project to identify, weight, and prioritize multiple attributes in the indication 'hepatitis c'. IQWiG Web site. https://www.iqwig.de/download/GA10-03_Executive-summary-of-working-paper-1.1_Conjoint-Analysis.pdf.
4. IQWiG. Contributing the patients' perspective. <https://www.iqwig.de/en/participation/contributing-the-patients-perspective.3070.html>. Accessed 5/27/2015.
5. NICE. Community engagement overview - NICE pathways. <http://pathways.nice.org.uk/pathways/community-engagement/community-engagement-approaches#path=view:/pathways/community-engagement/community-engagement-overview.xml&content=view-index>. Accessed 5/27/2015.
6. Mullin T. Patient focused drug development. PowerPoint presentation, June 20, 2012. <http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM310754.pdf>. Updated 2012. Accessed 12/2/2013.

7. Hoos A, Anderson J, Boutin M, et al. Partnering with patients in the development and lifecycle of medicines: A call for action. *Therapeutic Innovation & Regulatory Science*. 2015. doi: 10.1177/2168479015580384.
8. Boutin M. Advancing meaningful patient engagement in drug research, development, and approval.
<http://www.pharmacy.umaryland.edu/media/SOP/wwwpharmacyumarylandedu/centers/centersievents/pfdd/Boutin.pdf>. Accessed 6/2/2015.
9. Mullin T. FDA's patient-focused drug development.
<http://www.pharmacy.umaryland.edu/media/SOP/wwwpharmacyumarylandedu/centers/centersievents/pfdd/Mullin.pdf>. Accessed 6/2/2015.
10. Clinical Trials Transformation Initiative. Patient groups and clinical trials expert meeting (january 21-22, 2015). <http://www.ctti-clinicaltrials.org/what-we-do/ctti-projects/patient-groups/expert-meeting>. Accessed 9/2/2015.
11. National Health Council and Genetic Alliance. Advancing meaningful patient engagement in research, development, and review of drugs. washington, DC.
<http://www.nationalhealthcouncil.org/sites/default/files/PatientEngagement-WhitePaper.pdf>. Updated 2015/9/22.
12. Food and Drug Administration. Externally-led patient-focused drug development meetings.
<http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm453856.htm>. Accessed 11/2/2015.

13. Guidance for industry patient-reported outcome measures: Use in medical product development to support labeling claims. Food and Drug Administration Web site.
<http://www.fda.gov/downloads/Drugs/Guidances/UCM193282.pdf>. Updated 2009.
14. Food and Drug Administration. Roadmap to patient-focused outcome measurement in clinical trials.
<http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/UCM370174.pdf>. Accessed 6/2/2015.
15. Klein R. Patient representative program.
<http://www.pharmacy.umaryland.edu/media/SOP/wwwpharmacyumarylandedu/centers/centersievents/pfdd/Klein.pdf>. Accessed 6/2/2015.
16. Food and Drug Administration. About the FDA patient network.
<http://www.fda.gov/ForPatients/About/default.htm>. Accessed 6/2/2015.
17. Parent Project Muscular Dystrophy. Guidance for industry: Duchenne muscular dystrophy developing drugs for treatment over the spectrum of disease. . 2014.
18. Okun S, Murphy T. Patient *First* drug development: Exploring the patient perspective.
http://www.pharmacy.umaryland.edu/media/SOP/wwwpharmacyumarylandedu/centers/centersievents/pfdd/Okun_Murphy%20PFDD%20Final%2009Mar2015%20redacted.pdf.
Accessed 6/2/2015.
19. Brown C. Patient-focused drug development: The journal of the national PKU alliance.
<http://www.pharmacy.umaryland.edu/media/SOP/wwwpharmacyumarylandedu/centers/centersievents/pfdd/Brown.pdf>. Accessed 6/2/2015.

20. Beal A. Pharma's role in getting patients ready to partner in development.
<http://www.pharmacy.umaryland.edu/media/SOP/wwwpharmacyumarylandedu/centers/centersievents/pfdd/Beal.pdf>. Accessed 6/2, 2015.
21. Patient-Centered Outcomes Research Institute. Engagement rubric (updated February 11, 2015).
22. Schneider R. Patient-centricity: Making stone soup.
<http://www.pharmacy.umaryland.edu/media/SOP/wwwpharmacyumarylandedu/centers/centersievents/pfdd/Schneider.pdf>. Accessed 6/2, 2015.
23. Pfizer. Pfizer link. <https://www.pfizerlink.com/>. Accessed 6/2/2015.
24. Pfizer. Pfizer patient reported outcomes.
<http://www.pfizerpatientreportedoutcomes.com/>. Accessed 6/2/2015.
25. GetHealthy StayHealthy. <http://www.gethealthystayhealthy.com/>. Accessed 9/2/2015.
26. Patients to trials consortium. <https://sites.google.com/site/p2tconsortium/home>. Accessed 9/2, 2015.
27. Gatlin J. Remarks during interview at the M-CERSI conference on patient-focused drug development, March 9, 2015.
28. Perfetto EM, Burke L, Oehrlein EM, Epstein RS. Patient-focused drug development: A new direction for collaboration. *Med Care*. 2015;53(1):9-17. doi: 10.1097/MLR.0000000000000273 [doi].
29. Food and Drug Administration. The voice of the patient: Idiopathic pulmonary fibrosis. 2015.

30. Brookings Institute. Accelerating drug development for sickle cell disease.

<http://www.brookings.edu/events/2014/10/09-sickle-cell-disease-drug-development>.

Accessed 6/2/2015.

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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For further information on the conference, please visit:
www.pharmacy.umaryland.edu/patient_focused_drug_development

Appendix B. Example PFDD Meeting

The meetings elicit, using a semi-structure discussion format, patient perspectives on their disease, its impact on their quality of life, current approaches to treatment, and outcome preferences for future treatments and therapies (Appendix I, Table 1).²⁹ To date, FDA PFDD meetings have served to complement parallel scientific workshops, support development of disease-specific guidance, support efforts to develop new patient-reported outcome (PRO) measures, identify opportunities for further discussions (e.g., Brookings Institute discussions), and to identify new FDA Patient Representatives.^{9,30}

Table 1: Example PFDD Discussion Questions Used at FDA PFDD Meetings^{9,10}

| |
|---|
| <p>Symptoms and daily impacts that matter most to patients</p> <ul style="list-style-type: none"> ● Of all the symptoms that you experience because of your condition, which 1-3 symptoms have the most significant impact on your life? (Examples may include shortness of breath, cough, fatigue, etc.) ● Are there specific activities that are important to you but that you cannot do at all or as fully as you would like because of your condition? (Examples of activities may include household chores, walking up the stairs, etc.) <ul style="list-style-type: none"> ○ How do your symptoms and their negative impacts affect your daily life on the best days? On the worst days? ● How has your condition and its symptoms changed over time? |
| <p>Patient perspectives on treatment approaches</p> <ul style="list-style-type: none"> ● What are you currently doing to help treat your condition or its symptoms? (Examples may include prescription medicines, over-the-counter products, and other therapies including non-drug therapies such as diet modification.) <ul style="list-style-type: none"> ○ How well does your current treatment regimen treat the most significant symptoms of your disease? ● What are the most significant downsides to your current treatments and how do they affect your daily life? (Examples of downsides may include bothersome side effects, going to the hospital for treatment, etc.) ● Assuming there is no complete cure for your condition, what specific things would you look for in an ideal treatment for your condition? |