



Taking Stock of PFDD: Envisioning a Vibrant Future for Patient-Focused Drug Development

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PFDDworks is a collaborative forum for patient advocacy leaders to share learnings and advance understanding of how patient-focused drug development can be most effective and best deployed while ensuring that patient organizations remain at the forefront. PFDDworks is convened by Faegre Drinker Consulting and the Kith Collective.

When the Food and Drug Administration Safety and Innovation Act (FDASIA) was signed into law on July 9, 2012, expectations for one of its high-profile provisions—the Patient Focused Drug Development (PFDD) initiative—were modest. A commitment by the U.S. Food and Drug Administration (FDA) to host twenty meetings designed to “more systematically obtain the patient perspective on specific diseases and their treatments” could not have been predicted to catalyze such profound change—within the agency itself, among the patient

communities that have led and embraced the movement it fueled, and ultimately in how all medical products are developed and reviewed in the U.S. and potentially beyond.

Some may wait for solid “proof” of PFDD’s merits—a particular product approval, a label indication, or a coverage decision based on patient experience data—but those at the forefront see evidence of its deep and wide impact throughout the biomedical ecosystem. In the first half of this article, we examine these impacts.

This is a pivotal time for PFDD. Its full-scale adoption includes ways that truly improve individual and public health, and its very future depends on keeping patients and their caregivers at the center of PFDD. Our recommendations for making PFDD matter more and maintaining its authenticity follow in the second half of the article.

Impact on FDA

After being championed by FDA's Center for Drug Evaluation and Research (CDER) director Dr. Janet Woodcock, PFDD implementation has benefitted from the dedicated efforts of Dr. Theresa Mullin and her team. On a parallel path, Dr. Jeffrey Shuren, director of FDA's Center for Devices and Radiological Health (CDRH), was the force behind the Patient Preference initiative. CDRH identified an ambitious goal to make sure at least ninety percent of their staff have meaningful, direct contact with patients relevant to their agency work by the end of 2017. Infusing greater patient centrality throughout FDA was a high priority for the two most recent FDA commissioners, first Dr. Robert Califf and then Dr. Scott Gottlieb.

Here are just a few of changes resulting from these initiatives:

- These programs expanded ways for FDA to engage patients, caregivers, and advocates, giving them new venues and vocabulary for dialogues outside product-specific decisions and means to better understand their experiences, unmet needs, expectations, and preferences.
- FDA has recognized that what we can measure is not always what we *should* measure. The agency has underscored that symptoms and functional impairments that matter most to patients with a variety of serious conditions of high unmet medical need are often not the focus of sponsors' programs. In response, the FDA has begun pushing back against use of endpoints and outcome measures when they do not match what they have heard from patients.
- Agency expectations for patient experience data and utilization of it in decisions are becoming ever clearer

and harder for sponsors to ignore due to its public presentations, a series of workshops and draft guidances, and reports under the Patient-Focused Impact Assessment now included in product approvals.

Impact on Patient Advocacy Organizations

Although the “nothing about us without us” mantra of the disability rights movement stretches back to the 1960s, enactment of PFDD may mark the greatest shift for patient advocacy since HIV/AIDS activism reset both roles and tactics in the late 1980s and early 1990s.

We provide three examples of new patient advocacy frontiers opened by PFDD and related activities:

- While twenty PFDD meetings were initially planned, the combined success of and external interest in this program led to rapid-fire expansion of “externally led” meetings where advocacy organizations working on a single condition could jointly apply to FDA to host a meeting using a similar format. FDA review staff attend these meetings and resulting “Voice of the Patient” reports are posted on the FDA website as a resource for the agency, sponsors, and the public. Nearly fifty such meetings have been held to date and demand continues to be strong.
- Whether led by organizations inspired by their participation in the formal PFDD process or those that created other ways of bringing patient perspectives to the agency and sponsors, there is more interest than ever in preparing patients and caregivers for and engaging them in more direct roles to help prioritize research topics, evaluate proposals and study plans, co-design study materials, interpret study findings, draft regulatory

guidance, develop platform or master trials, assess medical product value, etc. A growing number of organizations host training events and programs to equip community members for these new opportunities. PFDD meetings now are often an element of an overall PFDD strategy, not simply a stand-alone event.

- With greater emphasis on gathering input from patients who reflect a broad spectrum of experience, organizations are pioneering new approaches to expand outreach and engagement beyond the connected core of their communities. They partner in new ways to better reach underserved groups, including ethnic and racial minorities, more severely affected individuals, those distant from specialty care and university-based clinical research centers, and people who may not view themselves as “patients,” such as at-risk individuals, people who have recovered or are survivors, and people outside the healthcare system.

The role of patient organizations is evolving to that of trusted convener of industry, agencies, and academia to advance components and the impact of PFDD in an open and transparent, pre-competitive environment.

Impact on Life Science Companies

Like other types of large-scale change, the attention paid to PFDD and related programs varies greatly across the industry landscape. There are signs of change and growing adoption as FDA and the European Medical Agency define new expectations for including the patient voice and alter their processes accordingly. Here are a few of them:

- Companies translate a new patient focus into internal training programs and hiring and retention practices to expose PFDD concepts to functions beyond those that have generally paid the closest attention—patient advocacy, outcomes assessment, and regulatory—bringing staff in early from R&D, clinical operations, market access, and commercial. Even some legal and compliance team members are taking note and helping colleagues structure contracting processes to better support robust patient engagement activities.
- Recognizing that many legacy Patient Reported Outcome Measures (PROMs) were developed on the basis of physician or academic investigators' observations, companies explore and invest to develop novel outcome measures that better align with patient experience and leverage digital and telehealth tools that can provide more direct and continuous measurement.
- In diseases where severe disability is present very early in life or where it develops in the later stages of life, the role of the caregiver as an engaged and reliable provider of observer reported outcomes is growing in acceptance as a critical and essential clinical outcomes assessment tool.
- There are an expanding number of pre-competitive arenas in which companies participate alongside patient advocates and academics to shape methods for the science of patient input and streamline development plans to reduce burdens for patients in clinical trials. Some of these take place at the broad systems level such as the European Union's Innovative Medicines Initiative PARADIGM project, while others address shared opportunities and challenges in a single condition and community

of interest. These are often formed and managed by patient advocacy organizations.

Recommendations

From a policy perspective, we see the upcoming Prescription Drug User Fee Act (PDUFA) VII as an important opportunity to strengthen PFDD both in terms of its rigor and accountability. PDUFA V and PDUFA VI, along with the 21st Century Cures Act, laid the statutory cornerstones for PFDD upon which a sustainable approach to the role of patient experience can be built. Emerging FDA draft guidances and other operational steps provide structure for these efforts. Our priorities for PDUFA VII fall into the following four topical areas.

Transparency

Our organizations, and various supporters, are making significant investments in developing robust patient and caregiver data to support PFDD strategies. We need to continue to improve awareness with sponsors of the need to incorporate patient perspectives early in target identification and clinical trial design and for both sponsors and regulators to appropriately share how they are using this information. The Patient-Focused Impact Assessment Act, incorporated into the 21st Century Cures Act, was an important step in this direction requiring FDA to publish a brief, post-approval statement on how patient experience data was used in the review of the product.

Our goals here are several-fold:

- 1) To enhance this reporting with earlier awareness in the product development cycle so that opportunities are captured across the product development continuum to ensure that what matters most to the patients is incorporated;

- 2) To advance opportunities to support and reflect in the label determinations that are made based in whole or in part on such patient experience data; and

- 3) To recognize the value of and advance patient-led, pre-competitive platforms that allow a robust interchange among patient groups, regulators, academic researchers, and drug developers, predicated on full transparency and recognition of complementary contributions and goals.

Authenticity

As noted above, initial PFDD projects (e.g., FDA-led and externally-led PFDD meetings) and sustained commitments to develop and deliver patient experience data are fundamentally altering how we pursue our mission to confront serious diseases. This is happening because we possess unique working relationships with our communities built on trust and unswerving dedication. At the same time, the drug development and regulatory review processes are highly complex and prone to following longstanding practices. We believe that there is a need to ensure the role of patient organizations in delivering authentic patient and caregiver perspectives is preserved as the growth of PFDD attracts, predictably, new players, independent vendors, and voices that may appear to speak for patients and caregivers but may have other interests at stake.

Consistency

As the PFDD infrastructure matures and becomes an increasingly reliable element of product review, it will be important to ensure that the science of patient input is used consistently across the FDA's centers, offices, and divisions. It is

understandable that any new paradigm requires formal processes and education to take root. Given the central role of PFDD in our future therapies, the necessary resources must be made available by Congress and the agency to implement these goals rapidly and consistently. Without this, we risk a growing divide between those areas where patient groups have resources to advance the field and those where these resources are lacking and an unmet need becomes even greater over time.

Comprehensiveness

Perhaps most importantly for the longer-term success of PFDD, its principles for patient-centered, data-driven product development must be applied across the entire new therapy discovery, development, and access continuum. It is

essential, but obviously not sufficient, for a new drug to demonstrate a clinically meaningful impact on what matters to patients. It must also become available to the appropriate patients in a timely manner. We encourage breaking down the barriers between marketing approval and market access—a gap which today is emerging as the second “valley of death” in the lifecycle of therapeutic development. This new evidentiary bridge from approval to access must be erected swiftly and with support of Congress, regulators, and payers. Payers must participate at an earlier stage to inform determinations of patient-centered clinical-meaningfulness in the context of regulatory review so these data have a direct line of sight into subsequent development of evidence of beneficiary value.

Patient-focused drug development is one of the single-most profound shifts in product development in decades. PFDD now provides the opportunity for patient advocacy organizations of all sizes to significantly accelerate development and deliver novel and more effective treatments to the people we serve. Focused effort and collaboration among stakeholder groups are required to ensure that it moves forward in a transparent, authentic, consistent, and comprehensive manner—with patient organizations remaining at the core of this area of regulatory science. We call on all stakeholders to join us in this commitment. **Δ**