FDA Patient-Focused Drug Development
External Resource Repository

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## Progression

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>• Guidance for Industry Patient-Reported Outcome Measures</td>
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<tr>
<td>2012</td>
<td>• FDASIA of 2012-- including PDUFA V Patient Focused Drug Development (PFDD) as a pilot to inform Benefit-Risk Assessment of new drugs</td>
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<tr>
<td>2013</td>
<td>• First PFDD meeting to hear from patients with Chronic Fatigue Syndrome</td>
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</table>
• Key learnings from first 3 years of PFDD meetings— informs patient stakeholders, Congress and FDA, including FDA negotiations for PDUFA VI  
• To expand on PFDD meetings FDA announces **option for an Externally-Led PFDD Meeting** |
| 2016 | • **21st Century Cures Act** -- including Sec 3002 Patient Focused Drug Development Guidance |
| 2017 | • FDA posts **Plan for Issuance of Patient-Focused Drug Development Guidance**  
• FDARA of 2017 including PDUFA VI Integrating Patient’s Voice into Drug Development  
• 21st CC PFDD Guidance 1 workshop |
| 2018 | • FDA launches webpage focused on **External Resources related to Patient Experience**  
• PFDD **Guidance 1 draft** guidance; **Guidance 2 and 3 workshops**; **Guidance 5 workshop**  
• FDA issues RFI to inform plans for work to support development of standard core COA sets |
Informing Benefit-Risk Assessment

• FDA makes regulatory decisions based on law and regulations
  – Decisions may be challenged in court and litigated

• Legal standard (for us): decisions cannot be “arbitrary and capricious” -- i.e., they must reflect a consistent policy, otherwise they are not fair

• Our decisions are our “case law”
  – Each decision is made either in the context of established policy or establishes new policy

• Decisions on B-R require judgment on the part of the regulator
## Basic Benefit-Risk Framework

<table>
<thead>
<tr>
<th>Decision Factor</th>
<th>Evidence and Uncertainties</th>
<th>Conclusions and Reasons</th>
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</thead>
<tbody>
<tr>
<td>Analysis of Condition</td>
<td>Sets the context for the weighing of benefits and risks:</td>
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<tr>
<td></td>
<td>• How serious is this indicated condition, and why?</td>
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<tr>
<td></td>
<td>• How well is the patient population’s medical need being met by currently available therapies?</td>
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<tr>
<td>Current Treatment Options</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benefit</td>
<td>Characterize and assess the evidence of benefit:</td>
<td></td>
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<tr>
<td></td>
<td>• How meaningful is the benefit, and for whom?</td>
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<tr>
<td></td>
<td>• How compelling is the expected benefit in the post-market setting?</td>
<td></td>
</tr>
<tr>
<td>Risk</td>
<td>Characterize and assess the safety concerns:</td>
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<tr>
<td></td>
<td>• How serious are the safety signals identified in the submitted data?</td>
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</tr>
<tr>
<td></td>
<td>• What potential risks could emerge in the post-market setting?</td>
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<tr>
<td>Risk Management</td>
<td>Assess what risk management (e.g., labeling, REMS) may be necessary to address the identified safety concerns</td>
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</table>
Patient-Focused Drug Development (PFDD) - 2012

• Patients are uniquely positioned to inform FDA understanding of the clinical context
• FDA could benefit from a more systematic method of obtaining patients’ perspectives on the severity of a condition, its impact on daily life, and their assessment of available treatment options
• PFDD initiative piloted a more systematic way of gathering patient perspective on their condition and treatment options
  – Under PDUFA V, FDA committed to convene at least 20 meetings on specific disease areas over the next five years
  – Meetings help advance a systematic approach to gathering input
# Patient Focused Drug Development (PFDD) Meetings

## Fiscal Year 2013
- Chronic fatigue syndrome/myalgic encephalomyelitis
- HIV
- Lung cancer
- Narcolepsy

## Fiscal Year 2014
- Sickle cell disease
- Fibromyalgia
- Pulmonary arterial hypertension
- Inborn errors of metabolism
- Hemophilia A, B, and other heritable bleeding disorders
- Idiopathic pulmonary fibrosis

## Fiscal Year 2015
- Female sexual dysfunction
- Breast cancer
- Chagas disease
- Functional gastrointestinal disorders
- Parkinson’s disease and Huntington’s disease
- Alpha-1 antitrypsin deficiency

## Fiscal Year 2016
- Non-tuberculous mycobacterial lung infections
- Psoriasis
- Neuropathic pain associated with peripheral neuropathy
- Patients who have received an organ transplant
- Alpha-1 antitrypsin deficiency

## Fiscal Year 2017
- Sarcopenia
- Autism
- Alopecia Areata
- Hereditary angioedema

## Fiscal Year 2018
- Opioid Use Disorder
- Chronic Pain
What We Ask in PFDD Meetings

**Burden of disease**

- Of all the symptoms that you experience because of your condition, which 1-3 symptoms have the most significant impact on your life?
- 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?
- How has your condition and its symptoms changed over time?

**Burden of treatment**

- What are you currently doing to help treat your condition or its symptoms?
- 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?
- What specific things would you look for in an ideal treatment for your condition?
Voice of the Patient Reports

• Each FDA PFDD meeting results in a summary report that captures the input from the various information streams
  – Faithfully summarizes participants’ experiences and perspectives, in their own voices
  – May include a sample of the B-R Framework’s first two rows, incorporating meeting input

https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/ucm368342.htm
FDA COA Compendium - 2015

• Information based on
  – Drug Labeling Approved From 2003 to 2014: December 31, 2014;
  – CDER’s DDT COA Qualification Program: December 31, 2015

• COA Compendium is a table that
  – Describes how certain clinical outcome assessments have been used in clinical trials to measure the patient’s experience (such as disease-related symptoms) and to support labeling claims.
  – Identifies clinical outcome assessments that have been qualified for potential use in multiple drug development programs under the COA type of the Drug Development Tool (DDT) Qualification Program of the Center for Drug Evaluation and Research (CDER).
Considerations

- **COA Compendium** (PDF) is a communication tool to be updated on a regular basis—includes COAs that have been used successfully in previous drug development programs
  - Not a comprehensive list of clinical outcome assessments and not intended to replace either existing disease-specific guidance or key interactions with FDA concerning drug development (e.g., during pre-IND meetings).
  - Drug sponsors are strongly encouraged to seek advice from the relevant Office of New Drug (OND) review division early in drug development to discuss the selection and implementation of the clinical outcome assessment specific to their program
  - Some of the clinical outcome assessments listed in the COA Compendium may be protected by proprietary rights, and in some cases, a royalty and fee may be charged by the copyright owners for their authorized use.
    - The inclusion of a clinical outcome assessment in the COA Compendium does not equate to an endorsement by FDA.
Externally-Led PFDD Meetings (2015)

• Respond to external stakeholder interest and expand opportunities to gather patient input on disease burden and treatment burden

• Meetings are conducted by external stakeholders (e.g., patient advocacy groups)
  – Meetings often target disease areas where there is an identified need for patient input on topics related to drug development
  – FDA’s PFDD meetings (agenda and facilitator questions) serve as model

• Meetings typically held locally in Washington metro area; FDA staff try to participate

• Meeting success will require a joint and aligned effort by all interested stakeholders

• For more information, please visit:
  http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm453856.htm
PFDD Learnings Emerging by 2015

- **Patients** with chronic serious disease are **experts** on what it’s like to live with their condition

- Patients “**chief complaints**” may not be factored explicitly into drug **development** plans, including measures of drug benefit planned in trials

- Patients want to be as active as possible in the work to develop and evaluate new treatments

- **PFDD** was intended to elicit broader patient input for a disease to better inform clinical context of BR assessment, but patient stakeholders were asking: **What’s next?**
  - Not expecting FDA to address all current gaps but want FDA to provide clear actionable guidance on what they and others need to do
  - Not wanting to duplicate efforts already undertaken by other groups—how to better share information
PFDD “What’s Next”: Need for guidance to enable stakeholders to go beyond powerful narrative and collect data that can serve as study endpoints and be used as a basis for marketing decisions.

<table>
<thead>
<tr>
<th>Dimension</th>
<th>Evidence and Uncertainties</th>
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<tr>
<td>Analysis of Condition</td>
<td>PFDD Meetings and Reports provide powerful narrative that gives regulators insights about clinical context and what matters to patients</td>
</tr>
<tr>
<td>Current Treatment Options</td>
<td></td>
</tr>
<tr>
<td>Benefit</td>
<td>Using measures &amp; tools (COAs) to systematically capture what matters most during clinical trials can turn narrative into evidence for regulatory decision making</td>
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<td>Risk</td>
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PDUFA VI: Enhancing Incorporation of Patient’s Voice in Drug Development and Decision-Making

• Conduct public workshops and develop series of guidance documents on:
  • Guidance 1: Collecting comprehensive patient-community input on burden of disease and current therapy (FY18)
  • Guidance 2: Development of holistic set of disease or treatment impacts most important to patients (FY19)
  • Guidance 3: Development of measures for an identified set of impacts (FY20)
  • Guidance 4: Clinical outcome assessments and better ways to incorporate COAs into endpoints (FY21)

• Repository of information on publicly available tools and ongoing efforts

• Conduct public workshop to gather experiences and recommendations of patients and caregivers on approaches to enhance engagement in clinical trials (FY19)

• Enhance staff capacity to facilitate development and use of patient-focused methods to inform drug development and regulatory decisions
FDA is posting links to externally generated reports and information on patient experience submitted to us for public sharing including reports from Externally-Led PFDD Meetings.
External Resources or Information Related to Patient Experience

1. Overview of CDER External Resource Webpage
2. Categories of External Resources
3. Frequently Asked Questions
4. Cover Page Guidelines

Webpage Link: https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm579132.htm
• Intended to **facilitate public discussion on patient-focused drug development and evaluation**

• Provides **links to certain publicly available** external reports and resources

• Serves as **resource** for patient community, patient advocates, researchers, drug developers, and federal agencies

• FDA reviews submissions to ensure materials are within scope -- **does not assess scientific merit or compliance with regulatory requirements**

• FDA decision to post links to these materials **does not reflect an endorsement**
Externally-led PFDD Meeting Reports or Other Stakeholder Meeting Reports

To help expand the benefits of FDA’s Patient-Focused Drug Development (PFDD) Initiative, FDA welcomes patient organizations to identify and organize patient-focused collaborations to generate public input on other disease areas. Submitted links to summary meeting reports from these externally-led PFDD meetings may be found here. FDA also welcomes submission of links to meeting reports from other stakeholder meetings collecting patient perspectives on disease burden and treatment burden.

- **Amyloidosis**
  In November 2015, the Amyloidosis Research Consortium hosted an externally-led Patient-Focused Drug Development meeting to hear directly from individuals living with systemic amyloidosis and their loved ones on the impact of amyloidosis on their daily lives, and their perspectives on approaches to treating amyloidosis.

- **Complement 3 Glomerulopathy (C3G)**
  In August 2017, the National Kidney Foundation hosted an externally-led Patient-Focused Drug Development meeting to hear directly from individuals living with C3G and their loved ones on the impact of C3G on their daily lives, and their perspectives on approaches to treating C3G.

- **Friedreich’s Ataxia**
  In June 2017, the Friedreich’s Ataxia Research Alliance hosted an externally-led Patient-Focused Drug Development meeting to hear directly from individuals living with Friedreich’s Ataxia and their loved ones on the impact of Friedreich’s Ataxia on their daily lives, and their perspectives on approaches to treating Friedreich’s Ataxia.
The proposed draft guidance relating to patient experience data that are listed here have been drafted and submitted by external stakeholders. As with other resources on the webpage, the proposed draft guidance and their content are not endorsed by FDA, and posting a link does not mean FDA has decided to adopt the proposed draft guidance.
### Natural History Studies or other Disease-specific Background on Condition and Discussion of Unmet Medical Need

Natural history studies track the course of disease over time, identifying demographic, genetic, environmental, and other variables that correlate with its development and outcomes in the absence of treatment. Website links to other publicly-available reports or documents providing disease-specific background on the condition and unmet medical need may also be found here.
FAQs are available for more information on scope and process

• What is Patient Experience Data?

• Who can provide a publicly available website link to a report or other resource?

• What types of resources will be included on this webpage?

• What types of resources will not be included on this webpage?

• How can you submit a publicly available website link to FDA?
Please include a cover page to promote transparency

- Title of resource
- Author(s) or Collaborator(s)
- Funding received or granted (if any)
- Version date
- Statement that the resource has not been revised or modified
- Statement that the resource can be linked from the FDA website
Submit Resources to: PFDDresources@fda.hhs.gov

For more information visit:
CDER’s Patient-Focused Drug Development Homepage

If you have questions, please email: patientfocused@fda.hhs.gov
Standard Core Clinical Outcome Assessments and Endpoints -- 2018

• In July 2018 FDA published a request for information (RFI) to inform structuring of a program to facilitate development of publicly available core set(s) of clinical outcome assessment (COA) measures and endpoints
  – Minimum list of impacts that matter most to patients and are likely to demonstrate change relating to disease burden, treatment burden

• Under envisioned program, qualifying third parties would conduct a process following a development protocol that provides for:
  – Consistent application of appropriate methods (e.g., new guidance)
  – Consideration and use of vetted publicly available measures
  – Milestones workshops engaging key stakeholders (e.g., patients, FDA and other regulators, HCPs, industry, HTA, payers, researchers)
  – Milestone work products, including resulting COA measures, to be made publicly available
Some Relevant Links

• Website for Externally-Submitted Information Resources related to PED
  – Our new external resources page

• Published plan for issuance of guidance under 21st CC Act Section 3002

• Guidance 1 “Collecting Comprehensive and Representative Input”

• Public workshops scheduled for Guidance 2 and Guidance 3.
  – https://www.fda.gov/Drugs/NewsEvents/ucm607276.htm

• FDA Standard Core Clinical Outcome Assessments and Endpoints –Request for Information (RFI) published July 2018
Thank you