Patient-Focused Drug Development:

Identifying and building needed data sources to integrate patients' perspectives in decision-making

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FDA Benefit-Risk Assessment for Regulatory Decision Making

- Qualitative approach that is grounded in quantification of various data elements. Made at the population level at time of marketing approval:
  - Benefits – Efficacy endpoints from controlled clinical trials
  - Risks – Harms reported in clinical trials and other sources (e.g., spontaneous adverse event reports)
- Evaluation of B-R is dynamic
  - Knowledge of benefits and risks evolves over product life-cycle
- Decisions on B-R require judgment on the part of the regulator and are influenced by:
  - Statutory/regulatory standards
  - Societal expectations
    - Personal values and perspectives

Patients' Perspectives Inform FDA's Benefit-Risk Assessment

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

Patient-Focused Drug Development

- Patients are uniquely positioned to inform FDA understanding of the clinical context
- FDA could benefit from a more systematic method of obtaining patients' point of view on the severity of a condition, its impact on daily life, and their assessments of available treatment options
  - Current mechanisms for obtaining patient input are often limited to discussions related to specific applications under review, such as Advisory Committee meetings
- Patient-Focused Drug Development initiative offered a more systematic way of gathering patient perspective on their condition and treatment options
  - 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

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Commitment in PDUFA V:
Patient-focused drug development meetings incorporating patient's voice to decision making

Fiscal Year 2013	Fiscal Year 2014	Fiscal Year 2015	Fiscal Year 2016	Fiscal Year 2017
• Chronic Fatigue Syndrome/ Myalgic Encephalo-myelitis • HIV • Lung Cancer • Narcolepsy	• Sickle Cell Disease • Fibromyalgia • Pulmonary Arterial Hypertension • Inborn Errors of Metabolism • Hemophilia A, B, and other Heritable Bleeding Disorders • Idiopathic Pulmonary Fibrosis	• Female Sexual Dysfunction • Breast Cancer • Chagas Disease • Functional Gastro-intestinal Disorders • Parkinson's Disease and Huntington's Disease • Alpha-1 Antitrypsin Deficiency	• Non-Tuberculous Mycobacterial Lung infections • Psoriasis • Neuropathic pain associated with peripheral neuropathy • Patients who have received an organ transplant	• Sarcopenia • Autism • Alopecia Areata • Hereditary Angioedema

Questions are asked about Symptoms and daily impacts that matter most to patients (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?
- What worries you most about your condition?

Questions are asked about Patient perspectives on current treatment approaches (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?
- Assuming there is no complete cure for your condition, what specific things would you look for in an ideal treatment for your condition?

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Voice of the Patient Reports

- Each 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
- Input could support other aspects of drug development, e.g.
  - Help identify of areas of unmet need
  - Develop clinical outcome tools (PROs, etc.) that better address patient needs

* https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/ucm368342.htm

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Some PFDD Learnings to Date

- 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
- For progressive degenerative diseases many patients/parents feel an ideal treatment would at minimum stop progression of their/their child's loss of function
- Patients want to be as active as possible in the work to develop and evaluate new treatments; they and caregivers are able and willing to engage via Internet, social media, and other means

PFDD Next Steps

- Engage wider community to discuss methodologically sound approaches that:
  - Bridge from initial PFDD meetings to more systematic collection of patients' input
  - Generate meaningful input on patients' experiences and perspectives to inform drug development and B-R assessment
  - Are "fit for purpose" in drug development and regulatory context
- Provide guidance
  - For patient communities, researchers, and drug developers
  - On pragmatic and methodologically sound strategies, pathways, and methods to gather and use patient input

Further integrating patient perspective into medical product development and decision making

Need to build in the patient's perspective starting in the translational phase

Translational	Clinical Studies	Pre-market review	Post-market
What impacts (burden of disease and burden of treatment) matter most to patients and how to measure them?	What aspects of clinical trials can be better tailored to meet the patients who (might) participate in the trial?	How to better integrate patient reported outcome data or elicited patient preferences into BR assessments?	How to best communicate the information to patients and prescribers?
•How do we ensure that we get input representative of the whole disease population?	*•Do endpoints planned for the trial include the ones that matter most to patients? Are the desired endpoints feasible?*	*•How can the patient-reported evidence be integrated and evaluated?*	*•How to convey info that helps facilitate patients' and clinicians' informed decision making?*
•What symptom or functions matter most to people with this disease?	*•Does the protocol facilitate (or discourage) enrollment or continued participation? Could that be improved?*	*•How to utilize elicited patient preference studies?*	*•How to convey uncertainty to inform and support clinical decision-making?*
•How to best measure? (endpoints, frequency, mode of reporting, etc.)	*•Do informed consent and other processes within the trial reflect the needs and preferences of people with that disease?*	*•How to factor in key uncertainties?*	
		•How could individual differences in patient experience (or preference) of benefit versus harm be considered?	

Series of Workshops and Issued FDA Guidance Planned for Next 4 Years

1. Collecting comprehensive patient community input on burden of disease and current therapy (FY 2018)
   - How to engage with patients to collect meaningful patient input?
   - What methodological considerations to address ?
2. Development of holistic set of impacts (e.g., burden of disease and burden of treatment) most important to patients (FY 2019)
   - How to develop a set of impacts of the disease and treatment?
   - How to identify impacts that are most important to patients?
3. Identifying and developing good measures for the identified set of impacts that can then be used in clinical trials. (FY 2020)
   - How to best measure impacts (e.g., endpoints, frequency..) in a meaningful way?
   - How to identify measure(s) that matter most to patients?
4. Incorporating measures (COAs) into endpoints considered significantly robust for regulatory decision making (FYY 2021)
   - Topics including technologies to support collection through analysis of the data


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