FDA's Patient-Focused Drug Development

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Regulatory Context

- *"To be approved for marketing, a drug must be safe and effective for its intended use."*

  -PDUFA V Draft Implementation Plan (Feb 2013)*

- What does it mean to be effective?
  - Demonstrates "substantial evidence that the drug will have the effect it purports or is represented to have under proposed labeled conditions of use" (21CFR314.125, 21CFR314.126)
- The meaning of "safe" is not explicitly defined in the statutes or regulations that govern approval
  - The safety of a drug is assessed by determining whether its benefits outweigh its risks

*http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM329758.pdf

Benefit-Risk Framework for human drug review

Benefit-Risk Summary and Assessment		
Dimension	**Evidence and Uncertainties**	**Conclusions and Reasons**
Analysis of Condition		
Current Treatment Options		
Benefit		
Risk		
Risk Management		

Provides the therapeutic context for weighing benefits and risks

Incorporates expert judgments about the evidence of efficacy and safety, and efforts to further understand or mitigate risk

FDA's Benefit-Risk Framework (column)

Benefit-Risk Summary and Assessment		
Dimension	**Evidence and Uncertainties**	**Conclusions and Reasons**
Analysis of Condition	For each dimension… **What is the key information/data that supports your conclusions:** • What you know (facts) • What you don't know (uncertainties and underlying assumptions)	For each dimension… **What are your overall conclusions about:** • The strength of the evidence • The clinical relevance and significance of the evidence • Any implications on the regulatory decision
Current Treatment Options		
Benefit		
Risk		
Risk Management		

FDA's Benefit-Risk Framework (rows)

Benefit-Risk Summary and Assessment		
Dimension	**Evidence and Uncertainties**	**Conclusions and Reasons**
Analysis of Condition **Current Treatment Options**	**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?	
Benefit	**Characterize and assess the evidence of benefit:** • How compelling is the expected benefit in the post-market setting? • How clinically meaningful is the benefit, and for whom?	
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**	

Patient-Focused Drug Development (PFDD)

- Establishing the therapeutic context is an important aspect of B-R assessment
  - Patients are uniquely positioned to inform understanding
  - Current mechanisms for obtaining patient input are often limited to discussions related to specific applications under review

- PFDD is part of FDA commitments under the fifth authorization of the Prescription Drug User Fee Act (PDUFA V)
  - FDA will convene at least 20 meetings on specific disease areas through September 2017
  - Meetings can help advance a systematic approach to gathering patients' input on their condition and treatment options

PFDD meetings for FY 2013-2017

Fiscal Year 2013	Fiscal Year 2014	Fiscal Year 2015	Fiscal Year 2016-2017
• Chronic fatigue syndrome/ myalgic encephalomyelitis • 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 gastrointestinal disorders *To be conducted* • Parkinson's disease and Huntington's disease (September 22) • Alpha-1 antitrypsin deficiency (September 29)	*To be conducted* • Non-tuberculous mycobacterial lung infections (October 15) *To be announced* • Alopecia areata • Autism • Hereditary angioedema • Patients who have received an organ transplant • Psoriasis • Neuropathic pain associated with peripheral neuropathy • Sarcopenia

PFDD Outcomes

- Each meeting results in a Voice of the Patient report that faithfully captures patient input from the various information streams
  - May include a sample of the B-R Framework's first two rows, incorporating meeting input
- Input can support FDA staff, e.g.:
  - Conducting B-R assessments for products under review
  - Advising drug sponsors on their drug development programs
- Input could support other aspects of drug development, e.g.:
  - Help identify areas of unmet need (e.g., clinical aspects of a disease that are not yet being addressed)
  - Develop clinical outcome tools (e.g., patient reported outcomes, PROs), that better address patient needs

Other Contributions of PFDD

- Complement scientific workshops
  - CFS/ME, Female Sexual Dysfunction, Chagas, Nontuberculous mycobacterial infections
  - Support development of disease-specific guidance
  - CFS/ME (draft guidance published March 2014)
- Support efforts to develop PRO tools
  - Multi-partner working group on PRO development for CFS/ME
- Identify opportunities for further discussions
  - Brookings workshop in follow up to Sickle Cell Disease meeting
- Channel patient engagement
  - Patient representatives identified for CFS/ME and HIV

Externally-Led PFDD Meetings

- There is external interest in expanded efforts to gather patient input in support of drug development and evaluation
- Meetings conducted by external stakeholders provide an opportunity to expand the benefits of PFDD
  - Meetings should target disease areas where there is an identified need for patient input on topics related to drug development
  - FDA's PFDD meetings can serve as a model
- For more information, please visit: http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm453856.htm

Some PFDD Learnings to Date

- Patients with chronic serious disease are experts on what it's like to live with their condition
- They are able to identify and articulate specific disease impacts (symptoms, loss of function) in concrete terms
- They can identify and articulate what is important to them regarding treatment benefit
  - For progressive degenerative diseases, many patients/parents feel an ideal treatment would at minimum stop progression of their/their child's loss of function
- Their "chief complaints" may not be factored explicitly into drug development plans
  - E.g., as endpoints and measures of drug benefit planned in trials

Some PFDD Learnings to Date (cont'd)

- They want to be as active as possible in the work to develop and evaluate new treatments
- They want their experience described using words that they consider to best describe how it feels
- They and their caregivers are able and willing to engage via the Internet, social media, and all other means at their disposal
- They aren't expecting for FDA to address all the gaps in current treatment or current approaches to drug development but do want FDA to help identify the most effective pathway for them to play major contributing role

FDA's role

- FDA's mission is to protect and promote public health by evaluating the safety and effectiveness of new drugs.
- While we play a critical role in drug development, we are just one part of the process. We do not develop drugs or conduct clinical trials.
- FDA recognizes that it is not the agency's role to lead much of the development work on specific tools for specific drug development programs
- However, we do play a constructive role in guiding, helping, or evaluating at some stages of the pre-clinical translational and later clinical development work

Principles that could guide development of an approach

- Include patient-identified disease impacts, and thus potential measures of benefit from the beginning of drug development
- Measure and report terms that are identified and ratified by patients themselves
- Translate identified key impacts and elements of disease experience into a vetted measurement set that would be made widely available

PFDD Potential Next Steps

Advance science of patient input

- 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

- To: patient communities, researchers, and drug developers
- On: pragmatic and methodologically sound strategies, pathways, and methods to gather patient and use input

Immediate Next Steps

- Continue fulfilling commitments for PDUFA V
- Further engagement and discussions with patients and other stakeholders in preparation for PDUFA VI

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