FDA’s Patient-Focused Drug Development Initiative and the Benefit-Risk Assessment Framework

A FasterCures Webinar
February 19, 2014
About FasterCures

- We are an action tank that works to improve and speed up the time it takes to get important new medicines from discovery to patients.

- We create opportunities and provide a platform for nontraditional allies to come together to share ideas and find partners.

- We work across diseases, sectors, and disciplines.

- We are a center of the Milken Institute.
It’s the tracks...
Finding Big Ideas in Small Spaces
• Loose affinity network of 60 nonprofit disease research foundations

• Created to tackle the challenges that cut across diseases through innovative partnerships

• Connected through TRAIN Central Station, an open-source web platform: www.train.fastercures.org
“Benefit-risk assessment requires participation from multiple scientific disciplines.”
Who’s logged on?

- Nonprofit: 47%
- Biotech/Pharma: 21%
- Academia: 7%
- Government: 5%
- Investor: 1%
- Other: 19%
- Investor: 1%
- Government: 5%
- Academia: 7%
- Biotech/Pharma: 21%

FasterCures
A CENTER OF THE MILKEN INSTITUTE
Speakers

Andrea Tan  
Office of Strategic Programs, Center for Drug Evaluation and Research, Food & Drug Administration

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Managing Director, Communications & Policy, FasterCures

MODERATOR
FDA’s Benefit-Risk Framework & Patient-Focused Drug Development

Andrea Tan & Pujita Vaidya
Office of Strategic Programs
FDA Center for Drug Evaluation and Research (CDER)

FasterCures Webinar
February 19, 2014
What’s on the regulator’s mind?

Adverse Event Incidence
Communication
Trial Design and Conduct
Risk of Products In Same Class
Clinical Relevance Of Endpoint
Expected Patient Compliance
Availability of Other Therapies
Treatment Effect
Nature of Disease
Trial Drop-outs
Serious Adverse Event Incidence
Off-Label Potential
Risk in Chronic Use
Restricted Distribution
Risk Management
Study Population
Statistical Significance
Relative Efficacy
Target Population
Medication Guides
Education
Labeling
Patient Preference
Efficacy in Subgroups

Uncertainty

10
What might help a regulator?

...a framework that moves them from here:

...to here:
Designing a more structured approach

• CDER’s goals for Benefit-Risk (B-R) assessment were two-fold:
  – External: better communicate the reasoning behind CDER’s decisions
  – Internal: ensure the “big picture” is kept in mind throughout a complex, detailed review

• CDER determined that a structured qualitative approach best fit its drug-regulatory needs
  – Reflects the reality that B-R assessment is a qualitative exercise supported by extensive analysis of evidence on benefit and risks
  – Rigorously communicates the basis for decisions, in words
  – Flexible to accommodate more complex supporting quantitative analyses that can aid expert judgment
CDER’s Benefit-Risk Framework

<table>
<thead>
<tr>
<th>Decision Factor</th>
<th>Evidence and Uncertainties</th>
<th>Conclusions and Reasons</th>
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Benefit-Risk Summary and Assessment
# CDER’s Benefit-Risk Framework

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<td>Sets up the clinical context for weighing benefits and risks</td>
<td>Incorporates expert judgments on evaluation of the efficacy and safety data and any risk mitigation plans</td>
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<td>Analysis of Condition</td>
<td>What are the facts and key data? What information don’t you have?</td>
<td>How should the data be interpreted? What are the implications for the regulatory decision?</td>
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Benefit-Risk Summary and Assessment
FDA’s commitments in the fifth authorization of the Prescription Drug User Fee Act (PDUFA V)

- Publish a 5-year plan that describes FDA’s implementation approach
- Revise review/decision templates and manuals
- Conduct two public workshops on B-R
- Develop evaluation plan to ascertain the impact of the B-R Framework
- Conduct 20 public meetings to get patient input on specific disease areas (Patient-Focused Drug Development)
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 offers a more systematic way of gathering patient perspective on their condition and treatment options
  - FDA will convene at least 20 meetings on specific disease areas over the next five years
  - Meetings can help advance a systematic approach to gathering input
Identifying Disease Areas for the Patient-Focused Meetings

- In September 2012, FDA announced a preliminary set of disease areas as potential meeting candidates
  - Public input on these nominations was collected through an online docket and a public meeting
  - FDA carefully considered these public comments and the perspectives of the review divisions at FDA
- 16 diseases were identified to be the focus of meetings for the first set of meetings: meetings during fiscal years (FY) 2013-2015
  - This set was published in the Federal Register in April 2013
- Another public process will be initiated in 2015 to determine the set of meetings for FY 2016-2017
Identifying Disease Areas: Criteria for Nomination

- Disease areas that are chronic, symptomatic, and affect functioning and activities of daily living
- Disease areas for which important aspects of that disease are not formally captured in clinical trials
- Disease areas for which there are currently no therapies or very few therapies, or the available therapies do not directly affect how a patient feels, functions, or survives
- Disease areas that reflect a range of severity
- Disease areas that have a severe impact on identifiable sub-populations (such as children or the elderly)
- Disease areas that represent a broad range in terms of size of the affected population
FY 2013 Meetings

- Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): April 25, 2013
- HIV: June 14, 2013
- Lung cancer: June 28, 2013
- Narcolepsy: September 24, 2013
FY 2014-2015 Meetings

- Sickle cell disease: February 7, 2014
- Fibromyalgia: March 26, 2014
- Pulmonary arterial hypertension: May 13, 2014

- Alpha-1 antitrypsin deficiency
- Breast cancer
- Chronic Chagas disease
- Female sexual dysfunction
- Hemophilia A, Hemophilia B, von Willebrand disease, and other heritable bleeding disorders
- Idiopathic pulmonary fibrosis
- Irritable bowel syndrome, gastroparesis, and gastroesophageal reflux disease
- Neurological manifestations of inborn errors of metabolism
- Parkinson’s disease and Huntington’s disease
Developing the Approach: Key Process Objectives

- Tailor each meeting: in planning each meeting, we consider unique characteristics of the disease context
  - Current state of drug development, specific interests of FDA review division, needs of patient population
  - Customize the meeting format and discussion questions
- Use effective formats and meeting style for collecting input
  - Obtain broad patient input
  - Faithfully capture patient views
  - Provide usable input for FDA assessments
- Use venues that are accessible and reliable
  - In person: patient panel, large group facilitated discussions, small group breakout sessions
  - Remote: interactive webcast and phone line
  - Docket comments through regulations.gov website
What questions to ask?
Symptoms and daily impacts that matter most to patients

- 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?
What questions to ask?
Patient perspectives on current treatment approaches

- 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?
Highlights from Past Meetings

• CFS/ME
  - Held back-to-back with a technical workshop; patients emphasized the severity of the condition and the effects of post-exertional malaise, or a “crash”

• HIV
  - Full day meeting, focusing on (1) current approaches to managing HIV and on symptoms experienced because of HIV or its treatment, and (2) perspectives on HIV Cure Research
  - Incorporated real-time “polling questions” and interactive webcast

• Lung cancer
  - In addition to main meeting topics, patients discussed the factors they take into account when making decisions about using cancer treatments
Highlights from Past Meetings

- Narcolepsy
  - First meeting on a rare disease; patients described the impact of the disease on daily life, the cyclical nature of symptoms, and importance of education and awareness
  - Incorporated phone participation from remote participants

- Sickle cell disease
  - Heard a broad range of patient perspectives, including pediatric patients
  - In addition to main meeting topics, patients discussed views on participating in clinical trials; patients also emphasized the need for increasing awareness about the disease
The Voice of the Patient Meeting Report

- Each meeting results in a summary report that faithfully captures the patient input heard
  - CFS/ME and lung cancer reports have been published*
- Reports draw from several sources of input:
  - Panel testimony and group discussion from the public meeting
  - Comments from the meeting webcast
  - Comments submitted to the public docket
- FDA staff can consider this input during and outside of review
- Input can also inform drug development more broadly (e.g., help identify of areas of unmet need, develop clinical outcome tools)

*http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm368342.htm
Lessons learned from Patient-Focused Drug Development meetings

- Patients, caretaker, and patient advocate perspectives have been powerful and insightful
- The meetings can be effectively tailored to fit the needs and interests of the patient community and FDA review divisions
- It can be a challenge to ensure that the input we get reflects the entire range of patients experiences and perspectives, and to hear from all patients during high turnouts
- Effective patient stakeholder engagement has been critical to the success of past meetings
- FDA has received positive feedback on the meetings and reports, both internally and externally
Speaker

Kim McCleary
Director, Strategic Initiatives,
FasterCures
It’s all relative...

“Understanding the Benefits and Risks of Pharmaceuticals: A Workshop Summary”
Institute of Medicine, 2006
Patient-Focused Drug Development

Eric Gascho
Assistant Vice President, Government Affairs
National Health Council
NHC’s Support for FDA User Fee Agreements

- Develop an objective, qualitative benefit-risk framework that includes robust patient input
- Expand the use of biomarkers, patient reported outcomes in clinical trials, and companion diagnostics
- Increase resources for Rare Disease Program
Patient Engagement in Regulatory Decision-Making

**Drug Development**
- Provide input on benefit-risk assessments, which are likely to evolve through the course of clinical investigations

**Approval**
- Serve on advisory committees to help inform FDA’s decision making
- Provide insight on patient-focused factors for consideration in assessments of benefit-risk

**Post-Market**
- Ensure balanced assessment of new information in weighing benefit-risk

- Patient advocacy, caregiver, and consumer organizations
- Individual patients, caregivers, and consumers
- Both
Patient Engagement in Research & Development Process

**Research Agenda**
- Provide feedback on relevance of research topic to patients, caregivers, and consumers
- Help identify new topics for research

**Development of Research Questions**
- Determine questions that are useful to patients, caregivers, and consumers and would have real-world applicability

**Selection of Outcomes and Comparators**
- Identify outcomes of interest to patients, caregivers, and consumers

**Recruitment**
- Help develop approaches to maximize potential for broad and meaningful representation of patients in research

**Translation and Dissemination**
- Help patients, caregivers, and consumers understand findings

Sources:
NHC Patient Information Tool

The Patient Information Tool consists of three sections:

- **Section I**: Identification of Subpopulations
- **Section II**: Description of Disease Diagnosis and Impact
- **Section III**: Description of Treatment and Management Options

Those applying the tool should be mindful of potential variances between patient and caregiver needs and preferences, as well as ensure that information from hard-to-reach populations is captured.
### Section 1: Identification of Subpopulations

<table>
<thead>
<tr>
<th>Considerations</th>
<th>Disease State and/or Stage Subpopulations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relevant segments might include age:</td>
<td>Relevant categories may include disease severity:</td>
</tr>
<tr>
<td>• Child</td>
<td>• Mild</td>
</tr>
<tr>
<td>• Adult</td>
<td>• Moderate</td>
</tr>
<tr>
<td>• Elderly Adult</td>
<td>• Severe</td>
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<tr>
<td></td>
<td>• End-of-Life</td>
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<tr>
<td></td>
<td>Other factors or predispositions (gender, race, occupation) that may be relevant to the condition</td>
</tr>
</tbody>
</table>
# Section 2: Description of Disease Diagnosis and Impact

<table>
<thead>
<tr>
<th>Considerations</th>
<th>Diagnosis</th>
<th>Impact on Subpopulations</th>
<th>Impact on Social Factors</th>
<th>Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• How diagnosed</td>
<td>• Incidence of disease</td>
<td>• Social factors impact on treatment decisions (e.g. ability to work)</td>
<td>Any existing/potential measures that could effectively evaluate:</td>
</tr>
<tr>
<td></td>
<td>• Existing diagnostic tests</td>
<td>• Prevalence of disease</td>
<td>• Role of family or caregivers in decision making</td>
<td>• Symptoms</td>
</tr>
<tr>
<td></td>
<td>• Prevalence of misdiagnosis/delayed diagnosis and impact on managing/treating condition</td>
<td>• Mortality rates</td>
<td>• Impact of condition and comorbidities on daily activities</td>
<td>• Function</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Variation in disease impact (e.g. across racial/ethnic groups)</td>
<td></td>
<td>• Quality-of-life</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Significant symptoms</td>
<td></td>
<td>• General health status</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Comorbidities</td>
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# Section 3: Treatment & Management Options

<table>
<thead>
<tr>
<th>Considerations</th>
<th>Availability</th>
<th>Effectiveness</th>
<th>Safety</th>
<th>Use</th>
<th>Access</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number/ availability of FDA-approved options</td>
<td>Effect of treatment</td>
<td>Side effects</td>
<td>Use of treatment and management options</td>
<td>Barriers or potential barriers to treatments</td>
</tr>
<tr>
<td></td>
<td>Options currently being used</td>
<td>How well they work in treating disease and/or symptoms</td>
<td>Severity of side effects</td>
<td>Changes in treatment use over time</td>
<td>REMS status</td>
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<tr>
<td></td>
<td>Symptoms addressed/not addressed</td>
<td>Heterogeneity in treatment effect</td>
<td>Impact of side effects on daily life and quality of life</td>
<td>Most significant downsides</td>
<td>Insurance coverage</td>
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<td>Impact of side effects on functional capacity</td>
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<td>Applied utilization management tools</td>
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DREAM8.5: Crowdsourcing Computational Challenges to Accelerate Medical Solutions

MARCH 26, 2014
1-2PM Eastern

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