The Voice of the Patient
FDA’s CFS and ME Patient-Focused Drug Development Meeting

Sara Eggers, PhD
Office of Program and Strategic Analysis
FDA Center for Drug Evaluation and Research

IOM Diagnostic Criteria for ME/CFS
January 27, 2014
Introduction

• CFS and ME is a serious disease or set of diseases for which there are currently no FDA-approved therapies
  – FDA shares in the commitment to facilitate the development of safe and effective drug therapies for CFS and ME

• On April 25, 2013, FDA held a public meeting to hear perspectives from patients with CFS and ME
  – The first meeting conducted as part of FDA’s Patient-Focused Drug Development initiative
  – Provided us (and others) an opportunity to hear directly from patients
  – Part of a larger workshop to explore important issues related to CFS and ME drug development
Discussion Topics

- Background on Patient-Focused Drug Development (PFDD)
- Overview of the CFS and ME PFDD initiative
- Highlights of patient input, particularly as it relates to disease symptoms and impacts on daily life
## CDER’s Benefit-Risk Framework

<table>
<thead>
<tr>
<th>Decision Factor</th>
<th>Evidence and Uncertainties</th>
<th>Conclusions and Reasons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analysis of Condition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current Treatment Options</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benefit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk Management</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Benefit-Risk Summary and Assessment**
### CDER’s Benefit-Risk Framework

<table>
<thead>
<tr>
<th>Decision Factor</th>
<th>Evidence and Uncertainties</th>
<th>Conclusions and Reasons</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Analysis of Condition</strong></td>
<td>Provides regulators with the therapeutic context for weighing benefits and risks</td>
<td></td>
</tr>
<tr>
<td><strong>Current Treatment Options</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Benefit</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Risk</strong></td>
<td>Incorporates expert judgments based on evaluation of the efficacy and safety data and the expected impact of efforts to reduce and further characterize risks</td>
<td></td>
</tr>
<tr>
<td><strong>Risk Management</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Benefit-Risk Summary and Assessment**
Patient-Focused Drug Development (PFDD)

- Patients are uniquely positioned to inform understanding of the therapeutic context
  - Current mechanisms for obtaining patient input are often limited to discussions related to specific applications under review

- PFDD offers a more systematic way of gathering patient perspective on their condition and treatment options
  - FDA is convening at least 20 meetings on specific disease areas in Fiscal Years (FY) 2013 - 2017
  - Meetings can help advance a systematic approach to gathering input
Patient-Focused Drug Development

Initiating the Process

• In September 2012, FDA announced a set of diseases as potential meeting candidates
  – Public input on these nominations was collected through a docket and at a public meeting held in October 2012
  – >4,500 comments were submitted, addressing 90+ disease areas

• 16 diseases areas were selected for fiscal years 2013-15
  – This set was published in the Federal Register in April 2013
  – Another public process will be initiated in 2015 to determine the set for fiscal years 2016-2017
Patient-Focused Drug Development

Identifying Disease Areas

- FDA sought diversity along the range of diseases encountered in our regulatory decision-making

- We focused consideration on disease areas that:
  - Are chronic, symptomatic, affect functioning/activities of daily living
  - Currently have few or no therapies, or the available therapies do not directly affect how a patient feels, functions, or survives
  - Have important aspects that are not formally captured in clinical trials
  - Reflect a range of severity
  - Have a severe impact on identifiable sub-populations (e.g., children)
  - Represent a range in terms of size of the affected population
Disease Areas Meeting in FY 2013-2015

FY 2013

- Chronic fatigue syndrome
- HIV
- Lung cancer
- Narcolepsy

FY 2014 – 2015

- Fibromyalgia
- Sickle cell disease

- Alpha-1 antitrypsin deficiency
- Breast cancer
- Chronic Chagas disease
- Female sexual dysfunction

FY 2014 – 2015 (continued)

- Hemophilia A, Hemophilia B, von Willebrand disease, and other heritable bleeding disorders
- Idiopathic pulmonary fibrosis
- Irritable bowel syndrome, gastroparesis, and gastroesophageal reflux disease with persistent regurgitation symptoms on proton-pump inhibitors
- Neurological manifestations of inborn errors of metabolism
- Parkinson’s disease and Huntington’s disease
- Pulmonary arterial hypertension
Patient-Focused Drug Development

Meeting Format

- Meetings follow similar design, tailored to disease context
  - E.g., current state of drug development, specific interests of the FDA review division, the patient population
  - Discussion topics elicit patients' perspectives on their disease symptoms and impacts, and on treatment approaches

- Input is generated in multiple ways:
  - Patient panel comments followed by facilitated discussion with patients in the audience
  - Web participants can submit comments and respond to poll questions
  - A federal docket allows for more detailed comments
• Each meeting results in a report that captures the patient input from the multiple streams

• This input will support FDA staff, e.g.:
  – When conducting B-R assessments for products under review
  – When advising drug sponsors on their drug development programs

• Input might support drug development more broadly, e.g.:
  – Help identify specific areas of unmet need in the patient population
  – Help identify potential outcome measures that could be developed for clinical trials
CFS and ME Meeting Overview

• The April 25th PFDD meeting was part of a 2-day workshop
  – Day 2 included more technical discussions with regulatory, industry, clinical and scientific experts on issues related to drug development
  – A separate report of Day 2 is underway

• The meeting discussion focused on the primary PFDD topics:
  – Disease symptoms and daily impacts that matter most to patients
  – Patients’ perspectives on current approaches to treating CFS and ME

• The patient and advocate community was very engaged:
  – ~70 patient and patient representatives attended the meeting
  – Many participated by web
  – The public docket received 228 comments
CFS and ME Summary Report

- The summary report posted on September 2013
  - It provides a narrative of the patients’ experiences and perspectives in a way that is accessible to FDA staff
  - It reflects the content of the meeting and docket submissions

- The report drew from several sources of input:
  - The facilitated discussion from the April 25th meeting
  - Comments from the meeting webcast
  - Comments submitted to the public docket
  - Two surveys that were conducted by stakeholders and submitted to the docket
Key Themes

• Many participants could pinpoint the specific time when their symptoms began

• They stressed that CFS and ME is much more than simply feeling fatigued
  – > 50 symptoms were reported – cognitive and physical manifestations
  – Post-exertional malaise (‘crash’) is an exacerbation of symptoms

• The disease can take a devastating toll on patients and families
  – Some reported still being able to function in society while others reported that they were virtually housebound, or bedbound
  – Many described themselves as successful professionals or students before, but who now struggle with many aspects of day-to-day living
Key Themes, continued

• Patients use a complex regimen of drug and non-drug therapies to treat their disease and manage their symptoms
  – Over 100 therapies were mentioned
  – Also mentioned was a range of diagnostic tools and biomarkers that clinicians have used to help treat their condition
  – Their treatments offer varying degrees of effectiveness
  – They are often associated with bothersome side effects, which can exacerbate other aspects of the disease

• Patients are desperate for research and development of CFS and ME treatments
  – At a minimum: Better relieve their most significant symptoms
  – Ideally: Address the underlying cause(s) of the disease
Most Significant Symptoms

Cognitive Impairment

• The most frequently described symptoms were a range of chronic impairments to cognitive functioning
  – General terms: “brain fog”, “impaired executive function”
  – Specific manifestations: disorientation, inability to process information, slowed reaction times, impaired memory, inability to find words, spatial disorientation

• They gave concrete examples of the impact on day-to-day life:
  – Inability to concentrate for longer than 15 – 20 minutes
  – Difficulty interacting with people or participating in social situations
  – Stressful decision making
Most Significant Symptoms

Fatigue

- Participants described in detail their experience with fatigue, lack of energy, weakness, exhaustion
  - Feeling drained, difficulty recovering strength
  - “Tired but wired”
  - Extreme, “bone-crushing” fatigue

- They described specific impacts:
  - Can’t stand for more than a few minutes / walk more than a few blocks / climb flight of stairs
  - Able to shower once in several days
  - Inability to be active further exacerbates weakness, fatigue and pain
Most Significant Symptoms

Sleep Dysfunction

• Many participants indicated that they suffer from insomnia, sleep disruptions, or “unrefreshing sleep”
  – They were among the most commonly cited symptoms identified in the submitted comments

• They described how sleep quality can exacerbate fatigue and other symptoms
  – Sleeping 10, 12 or more hours doesn’t necessarily help

• They commented on the challenge of finding treatments that can help them sleep without exacerbating fatigue
Most Significant Symptoms

Chronic Pain

• Many participants described chronic pain, in varying forms
  – Muscle, joint, eyes, neck, nerve
  – Headaches and migraines
  – “Whole-body pain”

• Participants expressed concern about the lack of knowledge about the fundamental causes of the pain
  – A few commented that they also have fibromyalgia but don’t attribute all of their pain to that condition

• They commented on the challenge of finding the right treatments for pain
Other Symptoms

• Sore throat and other flu-like symptoms
• Orthostatic intolerance, dizziness or other issues related to blood pressure drops
• Susceptibility to viral and other infections
• Sensitivity to light, sound, temperature and other stimuli
  – Limits ability to use computer or watch TV, go outside, or be in social situations
  – Requires darkness
• Gastrointestinal issues
• Blurred vision, eyesight problems
Post-exertional Malaise ("Crash")

- Participants described a crash as an incapacitating exacerbation of all symptoms
  - Can occur after even minimal exertion, without warning
  - Can lead to: exhaustion, intense physical pain, inability to eat, incoherency, blacking out and memory loss, and flu-like symptoms
  - Can result in dangerous situations – falling, blacking out, accidents

- They offered insight into:
  - The difference between “physical” and “cognitive” crashes
  - Variation in the duration of crashes – days, weeks, months, years
  - Triggers – poor quality sleep, infection, stress, weather, massage
  - Attempts to control crashes– constant monitoring, strict limits
“Best Days” vs. “Worst Days”

- Some docket commenters described their best vs. worst days
  - **Best days:** relief from symptoms; can take care of personal needs without assistance; can engage in social activity
  - **Worst days:** severe pain or weakness; confined to bed; require silence and darkness; require assistance with even basic personal care

- Results of the submitted surveys support these descriptions:

<table>
<thead>
<tr>
<th>Excerpt from Chu and Jason Survey</th>
<th>% of Respondents (N ≈ 550)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Best Days</td>
</tr>
<tr>
<td>“can do light housework” OR “can only work part-time or on some household tasks”</td>
<td>67</td>
</tr>
<tr>
<td>“bedridden”</td>
<td>3</td>
</tr>
</tbody>
</table>
Overall Impact on Daily Life

- “Operate at 25% of normal”
- “Legitimate fear” of overexertion -- “you will pay for it”
- Loss of careers or education opportunities
- Difficulty making plans or keeping commitments
- Increased isolation
- Toll on family
- Harsh financial difficulties
- Feelings of hopelessness, emptiness and despair
Concluding Thoughts

• CFS and ME is a debilitating disease that can have a devastating impact on a patient’s life

• The patient input strengthens our understanding of:
  – The specific symptoms that matter most to patients
  – The burden of CFS and ME on patients and their families
  – The range of treatments currently used to treat CFS and ME
  – How well those treatments currently meet patients’ needs

• FDA has received positive feedback, internally and externally
  – Key to success: the meaningful engagement and valuable input provided by patients and the patient community
Relevant Links

- Background on FDA Patient-Focused Drug Development and Benefit-Risk Assessment
  - [http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm326192.htm](http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm326192.htm)

- April 25 and 26 Workshop: Drug Development for CFS and ME
  - [http://www.fda.gov/Drugs/NewsEvents/ucm369563.htm](http://www.fda.gov/Drugs/NewsEvents/ucm369563.htm)

- CFS and ME Voice of the Patient Report