Stakeholder Collaboration to Improve Patient-Centered Drug Development

Sixth Annual
Patient-Reported Outcome Consortium Workshop

April 29 - 30, 2015 ■ Silver Spring, MD

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Session Participants

Moderator

- Ashley F. Slagle, MS, PhD – Clinical Outcome Assessment Qualification Scientific Coordinator and Endpoint Reviewer, SEALD, FDA

Presenters

- Janet Maynard, MD, MHS – Medical Officer Team Leader, Division of Pulmonary, Allergy, and Rheumatology Products, FDA
- Elektra Papadopoulos, MD, MPH –Acting Associate Director, Study Endpoints Team, SEALD, FDA
- Katarina Halling, MSc – Patient-Reported Outcome (PRO) Group Director, AstraZeneca
- Cynthia A. Bens – Vice President, Public Policy, Alliance for Aging Research

Stakeholder Collaboration to Improve Patient-Centered Drug Development

April 29, 2015

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Center for Drug Evaluation and Research (CDER)

Disclaimer and Disclosure

- This presentation is not intended to convey official US FDA policy, and no official support or endorsement by the US FDA is provided or should be inferred

- The materials presented are available in the public domain

- I do not have any financial interest or conflict of interest with any pharmaceutical company

Mission

- Center for Drug Evaluation and Research (CDER)
  - "CDER's mission is to protect and promote public health by helping to ensure that human drugs are safe and effective for their intended use, that they meet established quality standards, and that they are available to patients"

http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM376545.pdf

Patient-Focused Drug Development (PFDD)

- Establishing the therapeutic context is an important aspect of benefit-risk assessment
  - Patients are uniquely positioned to inform understanding of this context

- PFDD offers a more systematic way of gathering patients' perspectives on their condition and treatment options
  - FDA is convening at least 20 meetings on specific disease areas
  - Meetings can help advance a systematic approach to gathering input

PFDD meetings FY 2013-2015

Fiscal Year 2013	Fiscal Year 2014	Fiscal Year 2015
• 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 *To be conducted* • Functional gastrointestinal disorders (May 11) • Alpha-1 antitrypsin deficiency • Parkinson's disease and Huntington's disease

Some Questions at PFDD Meetings

- Which symptoms have the most significant impact on your daily life?... On your ability to do specific activities?
- How well does your current treatment regimen treat the most significant symptoms of your disease?
- What specific things would you look for in an ideal treatment for your condition?
- What factors do you take into account when making decisions about using treatments? …. Deciding whether to participate in a clinical trial?

PFDD Meeting Outcomes

- Each meeting results in a report that faithfully captures patient input from the multiple streams
  - http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm368342.htm
- This input can support FDA staff, e.g.:
  - Conducting Benefit-Risk assessments for products under review
  - Advising drug sponsors on their drug development programs
- The input might support drug development more broadly:
  - Help identify specific areas of unmet need in patient population
  - Help identify outcome measures that could be developed for clinical trials

Example: Chronic Fatigue Syndrome/Myalgic Encephalomyelitis

- CFS/ME is a complex, debilitating disease
  - The exact cause or causes of CFS/ME are unknown
  - It affects 1-4 million people in the U.S. (CDC)
  - Symptoms and severity vary widely from patient to patient, and include both cognitive and physical manifestations

- Currently, there are no FDA-approved therapies indicated to treat CFS/ME

http://www.cdc.gov/cfs/hcp.html

CFS/ME Workshop Overview
April 25-26, 2013

- Two-day workshop and public meeting
  - Broad engagement across stakeholders
- **Day 1**
  - Part of the FDA's PFDD initiative
  - Opportunity to hear directly from patients
  - Focused on PFDD topics:
    - Disease symptoms and impacts that matter most to patients
    - Patient's perspectives on current approaches to treatment
- **Day 2**
  - More technical discussion with regulatory, industry, clinical, and scientific experts on issues related to drug development

CFS/ME Key Themes

- CFS/ME is much more than simply feeling fatigued
  - > 50 symptoms were described– cognitive and physical manifestations
  - Cognitive effects (“brain fog”) received the most attention
  - ‘Fatigue’ ranged from “tired but wired” to “bone-crushing” exhaustion

- Treatment involves a complex regimen of drug and non-drug therapies
  - Over 100 therapies were mentioned
  - Treatments offer varying degrees of effectiveness
  - Treatments are often associated with bothersome side effects, which can exacerbate other aspects of the disease

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
- 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

CFS and ME Workshop Outcomes

- **Workshop Day 1 Summary**
  - The Voice of the Patient Report: Chronic Fatigue Syndrome and Myalgic Encephalomyelitis
  - http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM368806.pdf
- **Workshop Day 2 Summary**
  - http://www.fda.gov/Drugs/NewsEvents/ucm386705.htm
- **Draft Guidance for Industry—CFS/ME: Developing Drug Products for Treatment**
  - http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm388568.pdf
- **Working group for COAs for CFS/ME**

Guidance for Industry

Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis: Developing Drug Products for Treatment

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact Dr. Janet W. Maynard at 301-796-2300.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

March 2014
Clinical/Medical

16617dft.doc
03/06/14

- Published – March 10, 2014

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM388568.pdf

Unmet Medical Need

- Serious disease, no approved therapies
- FDA offers expedited programs for serious conditions:
  - Fast track designation
  - Breakthrough therapy designation
  - Accelerated approval
  - Priority review
- Draft Guidance for Industry: Expedited Programs for Serious Conditions—Drugs and Biologics
  - http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf

Efficacy Considerations

- Substantial evidence of efficacy in the enrolled patient population
- Efficacy endpoints: reflect the claimed clinical benefit related to how a patient feels or functions
- Demonstrate an acceptable risk-benefit profile

Potential Efficacy Endpoints

- **Symptoms**
  - Such as fatigue or other symptoms of CFS/ME
- **Other Domains**
  - Exercise capacity and post-exertional malaise
  - Function

Patient-reported outcomes (PROs)

- For CFS/ME, FDA will consider the use of symptom assessments that have been developed and evaluated in other conditions or novel instruments
  - Endpoint and PRO selection should be discussed with the division early in drug development

Drug Development in CFS/ME

- Drug development requires multiple partners
- FDA's role: advise on the regulatory standards for product approval
  - Draft Guidance on Drug Development for CFS/ME articulates the expectations for drug approval

- Next steps
  - Working group for CFS/ME
  - Ongoing stakeholder collaboration

Mission

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  - "CDER's mission is to protect and promote public health by helping to ensure that human drugs are safe and effective for their intended use, that they meet established quality standards, and that they are available to patients"

- Stakeholder collaboration and patient input are key to achieving the vision

http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM376545.pdf

Thank you

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April 29, 2015

Elektra Papadopoulos, MD, MPH
Acting Associate Director, Study Endpoints Team
Office of New Drugs
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Stakeholder Collaboration to Improve Patient-Centered Drug Development

Katarina Halling MSc
PRO Group Director
AstraZeneca

SIXTH ANNUAL
PATIENT-REPORTED OUTCOME CONSORTIUM WORKSHOP

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Collaboration with patients

- There are no obstacles for us to speak to patients
- More listening to and less of ”running an idea by” patients
- Listening to patients is critical so we address what is important and to generate the information patients need for their decision making and setting expectations
- What is important and relevant to patients is important to other stakeholders as well

Two examples of listening to patients

- Risk – benefit patient interviews
- PatientsLikeMe

Collaboration among Pharma

- The PRO Consortium has motivated us to be more collaborative and less protective
  - Instruments
  - Ideas
  - Learnings
  - Address outstanding research agenda items together

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Cynthia A. Bens
Vice President, Public Policy
Alliance for Aging Research

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Session Outline/Objectives

- Provide examples of how patient organizations have been engaging with FDA, the research community, and industry in unique ways

- Describe the importance of qualification to our work and the benefits of qualification to patients

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Alliance FOR AGING RESEARCH

WHO WE ARE

The Alliance for Aging Research is the leading non-profit organization dedicated to accelerating the pace of scientific discoveries and their application in order to vastly improve the universal human experience of aging and health.

www.AgingResearch.org

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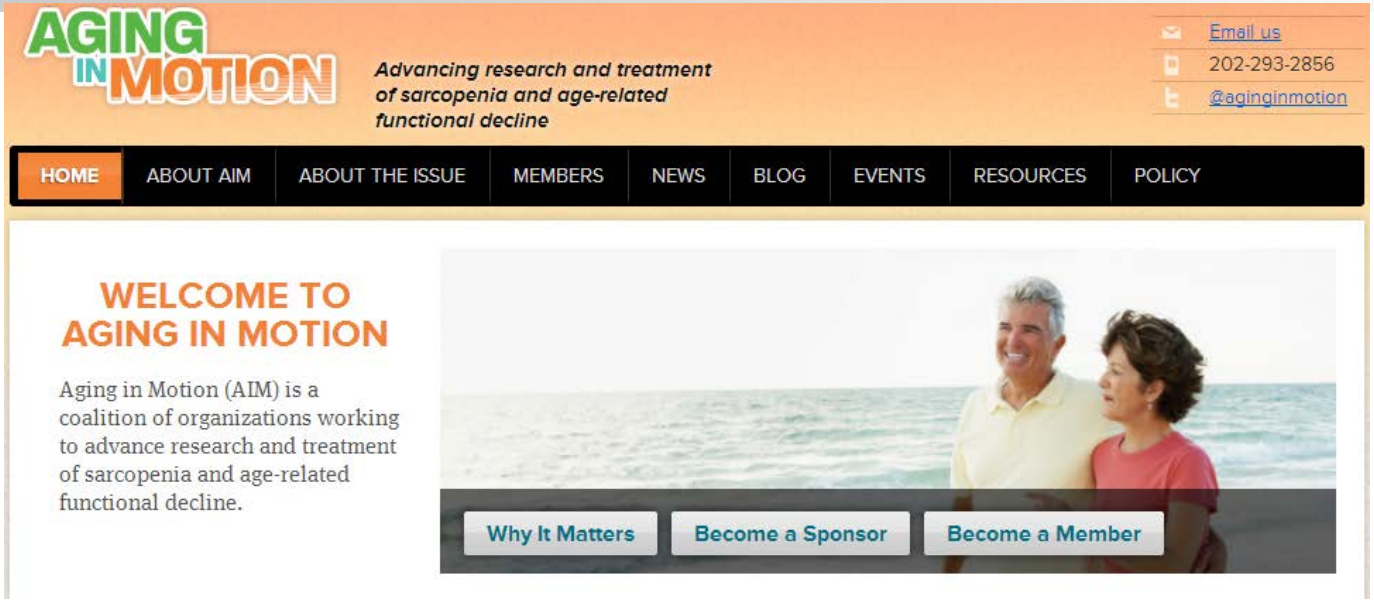

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

DDT COA 000037 **COMMENTS ON REVISED LETTER OF INTENT**

January 3, 2014

Alliance for Aging Research
Committee Head: Jack M Guralnik, MD, PhD, MPH
Professor of Epidemiology and Public Health
University of Maryland, School of Medicine
655 West Baltimore Street
Baltimore, MD 21201-1559

Dear Dr. Guralnik:

We have completed our review of the submission from the Alliance for Aging Research for DDT# 037, dated October 22, 2013, and received by the Clinical Outcomes Assessment (COA) qualification program via e-mail on October 23, 2013. The submission contains a Letter of Intent (LOI) that was revised based on comments provided in a CDER response letter dated August 27,

Based on your submission, we accept your proposal to submit further information to qualify Usual Gait Speed (UGS) and the Short Physical Performance Battery (SPPB) as performance outcome measures for use in still not fully specified drug-development contexts of use. This approval of your LOI for the qualification program advances this project to the Advice and Consultation stage. We look forward to your submission of an initial briefing package.

In discussing your revised LOI, the QRT had the following thoughts and observations:

- In your briefing submission, we encourage you to identify condition-specific patient populations. We are open to qualifying this instrument across more than a single condition. However, the range of conditions should begin with those that share similar lower-extremity muscle wasting manifestations. Going forward, it will also be important to consider what comorbidities should be among the exclusion criteria for trials using the measures.

- In refining the contexts where you see utility for UGS and SPPB, please consider the causal pathways through which disease and treatment affect performance on the tests. For example, results from a performance measure like the SPPB in trials for treatments aimed at a specific cancer-associated cachexia might have different meaning and thresholds for change than results from trials in a neurological condition, where disease-related alterations in kinesthesia might affect outcomes alongside muscle mass and strength changes. The