FDA Patient-Focused Drug Development

and why we are interested in Standard Core COAs

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5+ years of listening to Patients (e.g. PFDD Meetings) drives our interest in Core COAs

- Patients are uniquely positioned to inform FDA understanding of the clinical context
- PFDD meetings provided a more systematic method of obtaining patients' point of view on:
  - Burden of disease
  - Burden of available treatment
  - What patients would value most in a new treatment
- We've heard from patients in meetings spanning a wide range of conditions

PFDD Meetings conducted by FDA 2013-2018

2013	2014	2015	2016	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 **2018** • Opioid Use Disorder • Chronic Severe Pain

Key PFDD Learnings

- Patients with chronic serious disease are **experts** on what it's like to live with their condition
- The "chief complaints" heard in PFDD meetings often were not being factored explicitly into drug development plans, including measures planned for collection in trials
- Patients want to be as active as possible in the work to develop and evaluate new treatments

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Better integrating the patient's perspective at critical points in drug development and decision making

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 Benefit-Risk (BR) assessments?	How to best communicate the information to patients and prescribers?

Sustaining integration of the patient's perspective –making it a standard practice

- Ensure confidence in reliability and accuracy of patient experience data for regulatory decision making
  - Improve quality and reliability of submitted data (see guidance work)
- Promote rapid consistent adoption
  - Ensure review staff, industry, patients, and researchers are aware of new guidance, processes and available resources—lots of communication
- Reduce regulatory uncertainty for sponsor
- Sustained incorporation of patient's experience in drug development and decision making—make it standard practice
  - Lead and support development of publicly availably standard core set of COAs re: disease burden and treatment burden in a disease area

PFDD Guidance (21st Century Cures and PDUFA VI)

1. Collecting comprehensive patient community input on burden of disease and current therapy
2. Methods to identify what is most important to patients
3. Identifying and developing good measures for the identified set of impacts that can then be used in clinical trials.
4. Incorporating measures (COAs) into endpoints for regulatory decision making

5. Developing and Submitting Proposed Draft Guidance Relating to Patient Experience Data

FDA is also establishing a grant program to help make "Incorporating Patient Perspective" more sustainable

- Issue to be addressed:
  - There is currently little coordination in development of COAs including within a given disease area
  - Reviewers currently may see multiple independent efforts
    - Duplication of effort and diversity of measures and proprietary tools that limit affordability and sustainability
    - Variable quality of tools and resulting data that limit utility for regulatory decision making
- FDA grant program would enable development of standard core sets of measures of disease burden and treatment burden for a given area—that would be made publicly available

Standard Core Clinical Outcome Assessments and Endpoints Grant Program

- FDA **solicited applications for multiple grants** to support development of publicly available standard core set(s) of COAs and related endpoints
  - Minimum list of impacts that matter most to patients and are likely to demonstrate change relating to disease burden, treatment burden
- Conduct well-managed, transparent, and methodologically-sound process providing for:
  - Consistent application of appropriate methods (e.g., new guidance)
  - Consideration and use of vetted publicly available measures
  - Milestones workshops engaging key stakeholders (e.g., patients, FDA and other regulators, HCPs, industry, HTA, payers, researchers)
  - Milestone work products made publicly available

Focus of development of Standard Core COAs and Endpoints

- Focus on either a specified disease area or a disease impact that may span multiple disease areas, encouraging use of the following criteria:
  - Disease areas that are chronic, symptomatic, or affect functioning and activities of daily living
  - Disease areas that represent a broad range in terms of size of the affected population, including common conditions experienced by large numbers of patients and rare diseases that affect much smaller patient populations
  - Disease impacts that are relevant to patients' experience across a range of disease areas
- Interest in supporting development of standard core COAs relevant to disease conditions encountered in FDA decision making, and relevant to other regulators, health technology assessors and payers
- Interest in development of standard core sets of COA and related endpoints, not only for use in adults but also those for use in pediatric trials

Per those criteria, FDA identified the following areas of interest for development of COAs and endpoints

- For use in trials in **gastrointestinal diseases/conditions**, specifically for use across gastrointestinal diseases/conditions with overlapping signs and symptoms
- To assess **physical/functional status** including, but not limited to, standardized assessment of activities of daily living dependent on gross and fine motor function (including upper and lower limb function) across a range of diseases and populations
- For use in **migraine** trials, including functional impact or disability from migraine
- For use in trials of **opioid sparing drugs** intended to treat acute pain
- For use in **schizophrenia** trials, including but not limited to, shortened versions of current instruments, as appropriate

How does this relate to today's Oncology COA Workshop on analyzing physical function?

- CDER is advancing its PFDD efforts overall, including identification of core clinical outcome sets across diseases
- One core clinical outcome of interest across diseases is **physical function**
- Having a core outcome set is only a start, you still need a research objective
- Using a systematic approach like the estimand framework introduced in today's workshop, can generate regulatory-grade endpoints across therapeutic areas outside of oncology

Some Relevant Links

- Website for Externally-Submitted Information Resources related to PED
  - https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm579132.htm
- Published plan for issuance of guidance under 21st CC Act Section 3002
  - https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM563618.pdf
- Draft Guidance 1 "Collecting Comprehensive and Representative Input"
  - https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM610442.pdf
- Guidance 2 and Guidance 3 Public Workshop Materials
  - https://www.fda.gov/Drugs/NewsEvents/ucm607276.htm
- FDA Standard Core Clinical Outcome Assessments and Endpoints –Request for Applications (Deadline May 31, 2019)
  - https://grants.nih.gov/grants/guide/rfa-files/RFA-FD-19-006.html

Thank you!