

Novel Endpoints: A Regulatory Perspective

February 28, 2019

The 2019 Dermatology Innovation Forum

Elektra J. Papadopoulos, MD, MPH
Clinical Outcome Assessments Staff
Office of New Drugs

Center for Drug Evaluation and Research, FDA

Disclaimer

- Views expressed in this presentation are those of the speaker and do not necessarily represent an official FDA position.

Clinical Outcome Assessments Staff

- Mission:
 - Integrating the patient voice into drug development through clinical outcome assessment (COA) endpoints that are meaningful to patients, valid, reliable and responsive to treatment
- What we do:
 - Promote innovative, science-based review of COA development, validation, interpretation and communication of COA endpoints throughout the drug development life-cycle
 - Engage with internal and external stakeholders to advance good scientific COA standards and policy development
 - Address unmet medical needs by managing and leading the CDER's Drug Development Tool Clinical Outcome Assessment Qualification Program

Patient-Focused Outcomes

Those outcomes important to patients' survival, function, or feelings as identified or affirmed by patients themselves, or judged to be in patients' best interest by providers and caregivers when patients cannot report for themselves

*Donald L. Patrick, Ph.D., MSPH
May 20, 2013*

Clinical Benefit

- A ***positive clinically meaningful effect*** of an intervention, i.e., a positive effect on how an individual ***feels, functions, or survives***
 - How long a patient lives
 - How a patient feels or functions in daily life

- **Clinical outcome:** An outcome that describes or reflects how an individual feels, functions or survives
 - Assessed using clinical outcome assessments (COAs)

Highlights of 21st Century Cures and PDUFA VI

- 21st Century Cures and PDUFA VI increasingly places FDA as an *active participant* in drug development, broadening our traditional regulatory role
- Requires expanded efforts to enhance drug development
 - ***Patient-focused drug development: collect / analyze patient experience, to use in designing drug development programs (endpoints), and in regulatory decision making (endpoints and risk/benefit considerations)***
 - *Novel, innovative trial designs*: use of complex adaptive and other novel trial designs – and how such clinical trials can be used to satisfy the substantial evidence standard
 - *Real world evidence*: using data regarding use or potential benefits and risks of a drug derived from sources other than randomized clinical trials – in support of new indications and post-approval study requirements
 - ***Drug development tools: biomarkers and COAs***



FDA's Comprehensive Effort to Advance New Innovations: Initiatives to Modernize for Innovation

August 29, 2018

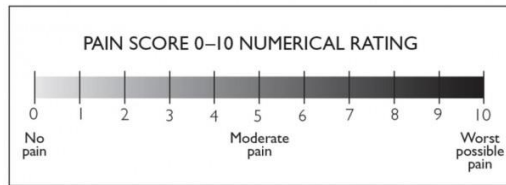
By: Scott Gottlieb, M.D.

- *“Electronic capture of PRO data (ePRO) is also becoming standard, providing a rich pipeline of structured clinical data.*
- *...mobile wearable technologies can complement traditional PRO surveys by generating objective, continuous activity and physiologic data.*
- *Obtaining reliable wearable device data on activity level, coupled with direct patient report on their ability to carry out important day to day activities, can provide information on physical function that is directly relevant and important....”*

How do we measure how patients feel and function?



Traditional Approaches



Novel Approaches





Some potential impacts of endpoints collected via remote data capture

- Enhancement of endpoints that matter to patients in daily life (e.g., information of patients' experiences between clinic visits)
- Reduced participation burden/fewer barriers to clinical trial participation (e.g., travel)
- Larger, more inclusive, and more generalizable trials



Digital health technology tools: Regulatory considerations for clinical outcome assessment

- Evidentiary considerations--broadly similar to other types of outcome measures
 - Is the assessment is ***well-defined*** and ***reliable***?
 - Does the endpoint score represents something meaningful to patients?
 - How much within-patient change in score/variable makes a difference in patients' lives?
- For continuous monitoring, defining meaningful endpoints can be challenging given the potential for large amounts of data

Some pathways for FDA engagement: Clinical Outcome Assessments



1

IND/NDA/BLA Pathway

Within an individual
drug development
program

Investigational New
Drug (IND) submissions
to FDA

Potential to result in
labeling claims

2

DDT COA Qualification Pathway

Outside of an individual
drug development program

Development of novel COAs
for use in multiple drug
development programs
addressing unmet
measurement needs

Potential to result in
qualification of COA

3

Critical Path Innovation Meetings Pathway

Outside of an individual
drug development program

Potential for *general CDER
advice* on specific
methodology or technology
(e.g., PRO instrument) in its
early stages of development

Meetings are informal, non-
binding discussions



Novel endpoint development in dermatology example: Alopecia areata

- COA Qualification—ongoing instrument development effort
 - PRO– “patient-reported symptoms and impacts of alopecia areata”
- FDA public meeting for patients and caregivers (Sept 11, 2017)
 - Meeting report “Voice of the Patient” issued March 2018
- Critical Path Innovation Meetings
 - Development of a Patient Reported Outcome Instrument for Alopecia Areata (April 2017)
 - Clinical Assessment Tools for Alopecia Areata (Dec 2017)

COA Staff



- Associate Director:
Elektra Papadopoulos, MD, MPH
- Regulatory Project Manager:
 - Kim Chiu, PharmD
 - Kristina Luong, PharmD
- DDT Qualification Scientific Coordinator:
 - Michelle Campbell, PhD
- Team Lead
 - Selena Daniels, PharmD, MS
 - Wen-Hung Chen, PhD
 - Sarrit Kovacs, PhD
- Reviewers:
 - Michelle Campbell, PhD
 - Yasmin Choudhry, MD
 - Ebony Dashiell-Aje, PhD
 - Onyekachukwu Illoh, OD, MPH
 - Julia Ju, PharmD, PhD
 - Susan Pretko, PharmD, MPH
- ORISE Fellow:
 - Prima Ghafoori, PharmD
 - Yujin Chung, PharmD

For more information

- **Clinical Outcome Assessment Qualification Program Webpage:**
 - <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm284077.htm>
- **Critical Path Innovation Meetings (CPIM):**
 - <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugInnovation/ucm395888.htm>
- **BEST (Biomarkers, Endpoints, and other Tools) Resource**
<https://www.ncbi.nlm.nih.gov/books/NBK338448/>
- **CDER: Patient-focused drug development webpage:**
 - <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm579400.htm>



Thank you!