ENGELBERG CENTER for
Health Care Reform
at BROOKINGS

Advancing Development and Use of Patient-Reported Outcomes in Drug Development: Near-Term Opportunities

Brookings Institution • Washington, DC
Monday, October 6, 2014

9:00 a.m. **Welcome, Overview, and Meeting Objectives**
Mark McClellan, Engelberg Center for Health Care Reform
Greg Daniel, Engelberg Center for Health Care Reform

9:15 a.m. **Opening Remarks**
Objective: Establish the context and goals for the expert workshop, highlight issues from key background documents

Speakers: Elektra Papadopoulos, Study Endpoints Team, OND, CDER, FDA

9:30 a.m. **Session Ia: Developing a Potentially Acceptable Endpoints List: Potential Value and Uses**
Greg Daniel, Moderator

Panelists:
Stephen Coons, Critical Path Institute
Robert Dworkin, University of Rochester
Katarina Halling, AstraZeneca
Naomi Aronson, Blue Cross Blue Shield

Objective: Outline and obtain feedback on the current FDA framework for identifying PRO instruments that are currently considered fit-for-purpose despite lacking formal qualification. Using two case studies, highlight the differences between a qualified measure and a "potentially acceptable" measure, and the benefits and challenges associated with making that distinction.

Potential topics:

- Discuss what "potentially acceptable" should mean, and how it might differ from "qualified"?
- What are key criteria that can be used to select "potentially acceptable" endpoints for inclusion on the list?
    - The current approach used to select potentially acceptable endpoints for the list is to identify instruments that have been used to support labeling claims. What are the relative merits and drawbacks of limiting the list to those instruments that have been successful in previous trials to support labeling claims only, versus including other assessments that appear to assess clinically meaningful concepts?
    - Is there a point during the instrument qualification process where the assessment could be considered for the acceptable endpoints list even though these instruments may lack documented success in previous trials?
    - What are the main concerns surrounding the fact that complete evidence and documentation supporting their measurement properties may not exist? How can we potentially address these concerns?

- What are the potential advantages and disadvantages of publishing a potentially acceptable endpoints list? For Industry? For Instrument developers (e.g., the PRO Consortium)? For patients? For payers?

10:30 a.m. **Break**

10:45 a.m. **Session Ib: Developing a Potentially Acceptable Endpoints List: Implementation Approaches**
Greg Daniel, Moderator

Panelists:
Dennis Turk, University of Washington
Ethan Basch, UNC-Chapel Hill
Josephine Norquist, Merck Sharp & Dohme, Corp.

- What are the possible approaches for identifying/collecting existing measures that are potentially acceptable?
    - What might be a feasible process for maintaining and periodically updating the list?
- Using the proposed table in the background package, does this best communicate the important information for these potentially acceptable endpoint measures?
    - If not, how might this table be adapted?

11:45 p.m. **Lunch**

1:00 p.m. **Session II: Identifying Emerging Themes from the Acceptable Endpoints Discussion**
Mark McClellan, Moderator

Objective: Reflect on the morning's discussion and identify the emerging themes that can be drawn from the case study examples

1:30 p.m. - 4:00 p.m. **Session III: Evidentiary Considerations for Making Existing PRO Instruments Fit for Purpose**

Objective: Drawing on hypothetical examples, explore approaches to and feasibility of adapting existing instruments to make them fit for use in clinical trials to provide evidence of treatment benefit. Discuss these approaches in the context of adapting them for 1) qualification and 2) inclusion on the potentially acceptable endpoint measures list.

Potential topics:
- Consider the following for both qualification and potentially acceptable endpoint measures:
- Content validity: what is enough? Published literature? New patient interviews? Saturation? Other methods?
- What types and level of evidence are needed to adapt an existing instrument to a new population?
- What evidence should be provided to modify key aspects of an existing instrument to make it fit for clinical trial use? Special consideration for:
    - Recall period
    - Add important items or remove items that do not measure treatment benefit

    - Remove attribution requirement (e.g., "How tired are you *as a result of your depression*?" modified to "How tired are you?")
    - Include additional instructions and/or add descriptors to item text to better define items
    - Modify scoring (e.g., separate items into different domain scores rather than using a total score)
- To what extent will adapting instruments be something that industry would embrace?
- How could the evidence be feasibly garnered within drug development timelines?
    - What is the ideal timing of submissions during drug development?
        - Qualitative evidence
        - Cross-sectional psychometric evidence
        - Longitudinal psychometric evidence
        - Interpretation of meaningful change
    - What possibilities exist for successful development and implementation of PRO endpoints when the ideal timeline has passed?
        - For example, could any aspects of psychometric validation be conducted during phase 3 studies? Could additional flexibility be afforded if the endpoint is a secondary endpoint versus a primary efficacy endpoint?

1:30 p.m. **Session IIIa: Evidentiary Considerations for Making Existing PRO Instruments Fit for Purpose**
Mark McClellan, Moderator

Panelists:
Charles Cleeland, UT MD Anderson Cancer Center
Bryce Reeve, UNC Lineberger Comprehensive Cancer Center
Lee Bowman, Eli Lilly
Jean Paty, Quintiles

2:45 **Break**

3:00 **Session IIIb: Evidentiary Considerations for Making Existing PRO Instruments Fit for Purpose, cont.**
Mark McClellan, Moderator

Panelists:
Arthur Stone, University of Southern California
Jason Lundy, Critical Path Institute
Glenn Kroog, Bristol-Myers Squibb
Alicyn Campbell, Genentech

4:00 p.m. **Session IV: Identifying and Prioritizing Next Steps**
Mark McClellan, Moderator

Objective: Identify and prioritize for action other outstanding research questions that have hindered the development of and confidence in many PRO assessments in clinical trials for regulatory purposes. These research questions may be explored in smaller subsequent workshops or in other venues.

Potential questions to consider:

- How can PRO data be appropriately applied in open label studies?
- What are acceptable methods for determining a clinically meaningful change?
- What are the key considerations in using instruments that allow patients to select their own most bothersome symptom(s) (e.g., Osphena (ospenifene) approval) when symptoms vary across individuals with a disease or condition?

4:30 p.m. **Closing Remarks**

4:45 p.m. **Adjournment**