One Approach to Filling Measurement Gaps for PRO Endpoints

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Financial Disclosures

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S – Critical Path Institute (C-Path)

Critical Path Institute (C-Path)

- Established in 2005 by the University of Arizona and the FDA's Center for Drug Evaluation and Research (CDER)
- Dedicated to implementing FDA's *Critical Path Initiative*
- An independent, non-profit organization
- Provides a neutral, pre-competitive venue for collaboration aimed at accelerated development of safe and effective medical products

Patient-Reported Outcome (PRO) Consortium

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- Formed in late 2008 by C-Path, in cooperation with FDA/CDER and the pharmaceutical industry
- Membership
  - Only available to medical product companies
  - 25 members in 2013 (all pharmaceutical firms)
- Non-Voting Participants
  - Representatives of governmental agencies
  - Clinical consultants, patients, academics, and CROs partnering in PRO instrument development

PRO Consortium

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Mission Statement

To establish and maintain a collaborative framework with appropriate stakeholders for the development of qualified, publicly available PRO instruments for use in clinical trials where PRO endpoints are used to support product labeling claims.

PRO Consortium

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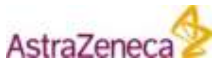
Goals

- Support pre-competitive collaboration that includes FDA input/expertise
- Facilitate FDA's review of drugs and biological products by standardizing PRO endpoints
- Avoid development of multiple PRO instruments for same purpose
- Share costs of developing new PRO instruments
- Develop qualified, publicly available PRO instruments

PRO Consortium Members



Funding

C-Path

- Government agency grants (e.g., FDA's CDER)
- Foundation grants/contracts (e.g., Gates)
- Private philanthropy
- Membership fees from member firms

PRO Consortium

- Scientific staff – CDER grant to C-Path
- Support/Project management staff – Membership fees
- PRO instrument development activities – Funded by the firms participating in the working groups ($750K to $2M over three to six years)

PRO Consortium

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Current Working Groups

- Asthma – 11 firms
- Cognition – 9 firms
- Functional Dyspepsia – 3 firms
- Irritable Bowel Syndrome (IBS) – 3 firms
- Lung Cancer (NSCLC) – 6 firms
- Rheumatoid Arthritis – 5 firms
- Depression – 8 firms

Working Groups

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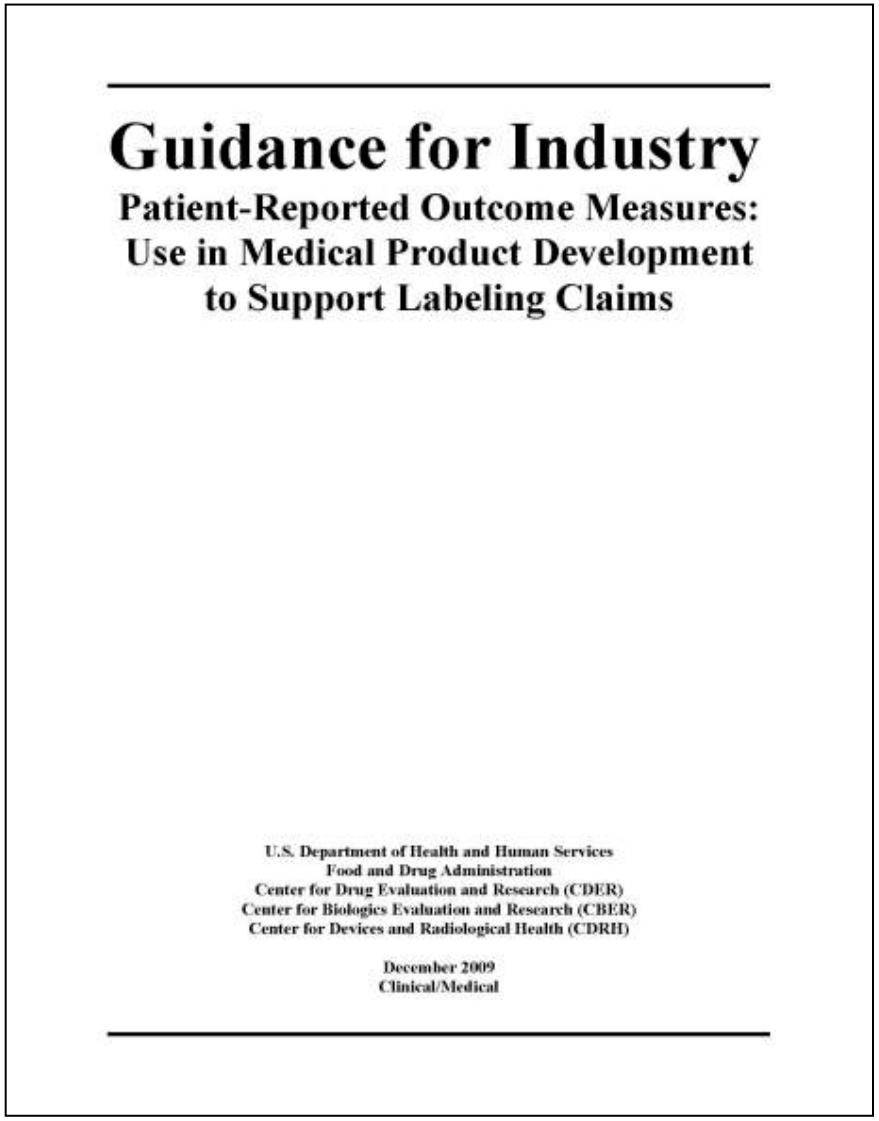
Goal

To produce and/or compile the necessary evidence to enable new or existing PRO instruments to be qualified by CDER for use in clinical trials where PRO endpoints can be used to support product labeling claims.

Note: Preliminary versions of PRO instruments have been submitted to CDER for initial review by the asthma, cognition, depression, and IBS working groups

FDA's "PRO Guidance"



Guidance for Industry

Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

December 2009
Clinical/Medical

Clear acknowledgement of the importance of appropriately and effectively incorporating the patient's voice into the evaluation of medical products

Released by CDER, CBER, and CDRH

Draft: February 2006

Final: December 2009

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM205269.pdf

Clinical trial endpoints for assessing treatment benefit

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- Survival
- Biomarkers (e.g., intraocular pressure)
- Clinical Outcome Assessments (COAs)
  - Patient-Reported Outcomes (PROs)
  - Observer-Reported Outcomes (ObsROs)
  - Clinician-Reported Outcomes (ClinROs)
  - Performance (e.g., sensory [e.g., visual acuity, visual field], motor, cognition)

Burke and Walton, 2011

An Industry Perspective
(Risa Hayes [Lilly] at the FDA on 12/2/10)

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PRO Consortium

- Involvement of FDA personnel early and throughout the process is critical
- Interaction with FDA has been invaluable
- Provides a…
  - novel approach to PRO instrument development
  - source of creativity and new ideas
  - critical mass of experts (from industry, FDA, C-Path, and others) with different skill sets and experiences
  - forum for discussion of frequently asked questions

PRO Consortium: Challenges

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- Gaining consensus within working groups regarding concepts of interest and context of use
- Retaining focus on symptoms
- Juggling different budget periods/fiscal years across multi-company projects
- Executing project agreements with member firms in a timely manner
- Instrument development and qualification is likely to take longer than the time it would take an individual company to develop a PRO instrument

Unique Challenges for the Device Industry

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- Most device firms are much smaller than firms in the pharmaceutical sector
- Many device firms are focused on one device or technology
- Device development timelines often shorter than pharmaceuticals
- PRO instruments rarely used to measure primary endpoints in pre-approval device trials
- Limited experience with pre-competitive, multi-stakeholder initiatives of this type (although MDIC is attempting to change this)

CDRH's "MDDT Guidance"

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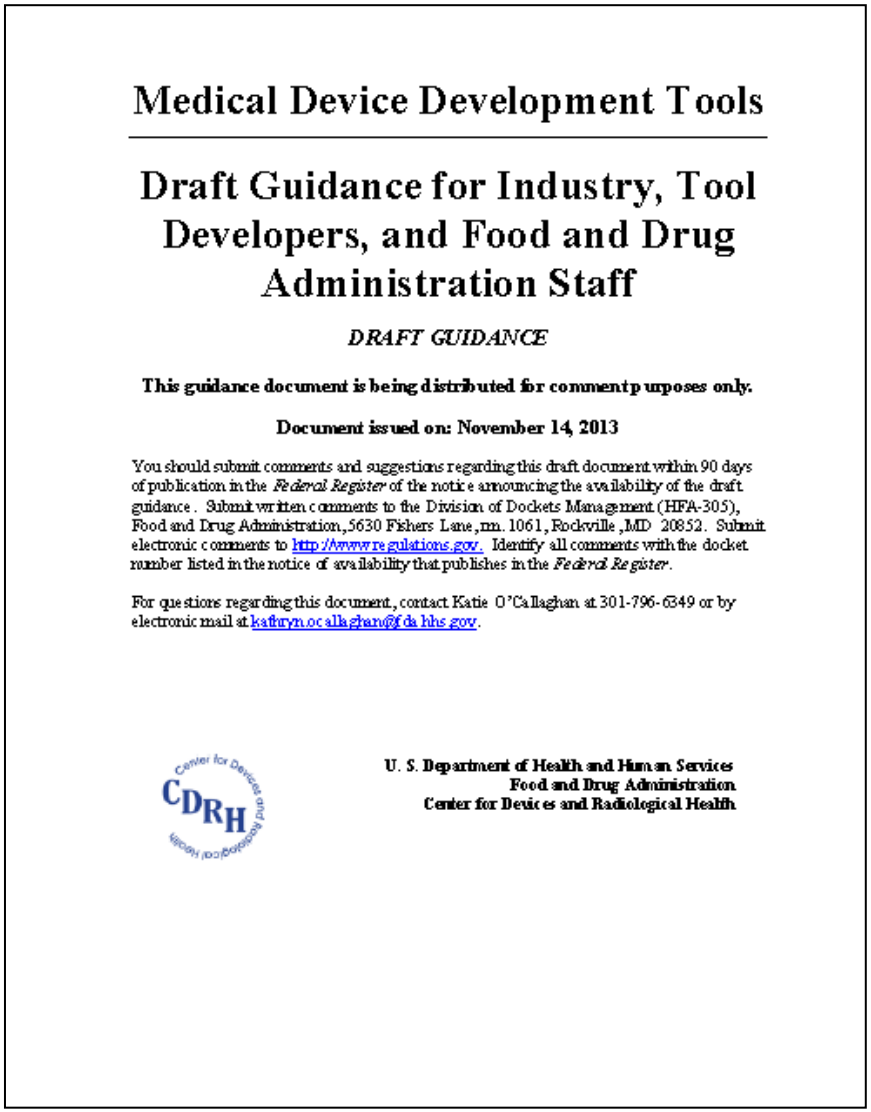

Medical Device Development Tools

Draft Guidance for Industry, Tool Developers, and Food and Drug Administration Staff

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Document issued on: November 14, 2013

You should submit comments and suggestions regarding this draft document within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.regulations.gov. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this document, contact Katie O'Callaghan at 301-796-6349 or by electronic mail at kathryn.ocallaghan@fda.hhs.gov.

U. S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Describes the framework and process for voluntary CDRH qualification of medical device development tools (MDDTs).

Released by CDRH

Draft: November 2013

http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM374432.pdf

Summary

- A pre-competitive PRO instrument development and qualification collaboration has been established
- CDER, through its Drug Development Tool (DDT) Guidance, has agreed to a structure for review and qualification of DDTs
- The process continues to be refined and improved as stakeholders learn what works and what doesn't
- CDRH now has a voluntary process for qualification of MDDTs for use in device development programs
- CDRH encourages the formation of pre-competitive, collaborative groups to foster MDDT development and qualification