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FDA Perspective on the Need for a PRO Consortium

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Presentation Overview

- Measuring treatment benefit:
Capturing the patient's perspective
- Developing PRO measures:
How can we be more efficient?



Treatment Benefit

- *Treatment benefit* — The impact of treatment on how a patient survives, feels, or functions as a result of treatment
- With few exceptions, other treatment impacts are surrogate measures and may not represent true treatment benefit
 - Exception: blood pressure



Evidence of Treatment Benefit: Requirements for Drug Claims

Evidence of drug effectiveness is deemed **substantial** for claims in product labeling (prescribing information, PI) if supported by **adequate & well-controlled** clinical trials using endpoint assessments that are **well-defined and reliable** to measure the specific concept(s) stated or implied by the claims.

Adapted from 21 CFR 201.57(c)(2)(iv) and (v)
21 CFR 201.80(c)(2)

*Labeling must be **not false or misleading in any particular.***



Characteristics of an *Adequate and Well-Controlled Study*

21 CFR 314.126 (b):

1. Clear statement of objectives
2. Study design permits valid comparison (appropriate control)
3. Select patients with disease/condition (treatment) or at risk of disease (prevention)
4. Baseline comparability (randomization)
5. Minimize bias (blinding, etc.)
6. **Appropriate methods for assessment of outcome**
7. Appropriate methods of analysis



Well-defined and Reliable Endpoints

- 21 CFR 314.126(b)(6)
 - *“The methods of assessment of subjects’ response are **well-defined and reliable**. The protocol for the study and the report of results should explain the variables measured, the methods of observation, and the criteria used to assess response.”*



Measurement of the Patient Perspective Is **Critical**

- Some of the most important treatment effects are known **only** to the patient
 - e.g., symptoms such as pain
- Only patients can adequately describe their experience/perspective



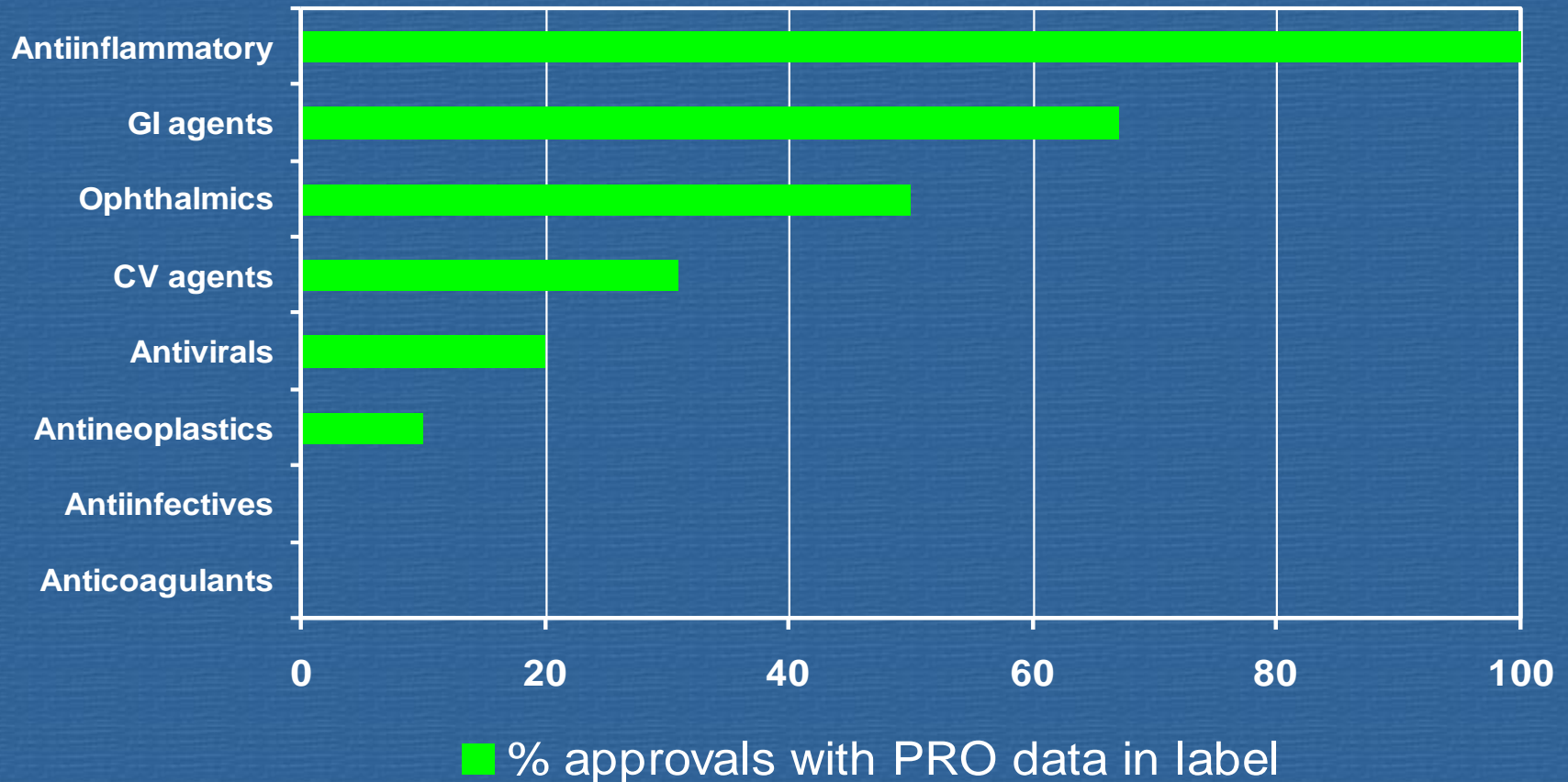
Patient-Reported Outcomes (PROs)

- A PRO is any report coming directly from patients, without interpretation by physicians or anyone else, about how the patient functions or feels in relation to a health condition and its therapy
- PROs have different format options
 - Questionnaire
 - Diary
 - Event log
 - Interview script



PROs in Drug Labeling

- Interest in patient reports is not new



(Willke et al, CCT, 2004)



PROs in Drug Labeling

- What is new is that direct patient reports of their experience of symptoms is preferred when possible--without the physician filter in place
- Surrogate endpoints alone may not represent treatment benefit
 - Hemoglobin
 - HbA1c
 - Serum Sodium
 - Radiographic Evidence of Disease
 - Tumor Size

None of these describe how a patient feels, functions, or survives as a result of treatment



Guidance for Industry

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

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 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 Laurie Burke (CDER) 301-796-0700, Toni Stifano (CBER) 301-827-6190, or Sahar Dawisha (CDRH) 301-594-3090.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
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2006.

Final version
currently going
through clearance
process....

No major policy
revisions expected.

Will clarify draft in
response to
comments.



Purpose of the PRO Guidance

- To confirm that FDA recognizes the importance of the patient perspective where appropriate
- To explain how FDA evaluates PRO instruments for their usefulness in measuring treatment benefit
- To explain FDA's evidence requirements when PRO instruments are used to support claims



When Is a PRO Instrument “Fit for Purpose?”

- Content validity is established for the purpose
 - Measurement concept matches targeted claim
 - Item content derived with target population input and is demonstrated to be valid in that population
- Construct validity, reliability and ability to detect change are adequate to support interpretation of clinical trial results



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Current Issues

- Lengthy instrument development process
 - Instrument development must begin in early stages of product development
 - No guarantees that the product will succeed
 - Many instruments are never fully developed
- Intellectual property concerns
 - Sharing between sponsors
 - Publication of instrument development documentation
- Expense
 - Each sponsor incurs significant cost in developing their own instrument
 - FDA staff review several instruments for same concept



A New Approach

- Collaborative effort is needed:
 - Private/Public Partnership
 - Reduce duplication of effort
- Consortium: an efficient approach for sponsors and FDA
 - Third party neutral ground
 - Timely
 - Less costly
 - Open communication (e.g., development process is in public domain)



Consortium Advantages

- Novel, efficient process for PRO instrument development
- Reduced duplication of effort
- Process and product (instruments) in the public domain
- Collaborative effort
- FDA participation throughout the process
- Improved labeling



Summary

- The Consortium will expedite PRO instrument development and ultimately drug development
- The Consortium will provide a forum for scientific exchange related to PRO instrument development
- FDA is committed to participate in PRO Consortium projects that will support product development and labeling

