

# Perspectives on Mixed Methods to Assess Content Validity of a PRO Measure

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# Use of Mixed Methods to Assess and Assure Content Validity: The PRO Consortium Perspective

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# PRO Consortium: Members



# PRO Consortium: Goals

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

# PRO Consortium

Criteria for selection of specific PRO instruments for development

- Disease/condition with unmet measurement need and a priority area for the member firms
- Disease/condition with regulatory 'demand' for pre-competitive PRO instruments based on feedback from FDA
- Disease/condition currently reliant on more 'objective' measurement where subjective impact of disease via PRO assessment should be assessed

# PRO Consortium Working Groups

- Asthma
- Cognition (mild cognitive impairment due to AD)
- Depression
- Functional Dyspepsia
- Irritable Bowel Syndrome
- Lung Cancer (NSCLC)
- Rheumatoid Arthritis

# Goal of Each Working Group

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

# FDA Qualification

- Qualification is based on an FDA review of evidence that supports the conclusion that a PRO instrument provides a **well-defined and reliable assessment of a targeted concept in a specified context of use.**
- FDA's *Guidance for Industry: Qualification Process for Drug Development Tools* (draft - October 2010)



# PRO Instrument Qualification

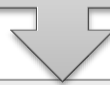
**...has the potential to:**

- More effectively incorporate the patient's voice into the evaluation of treatment effects
- Increase number of accepted PRO measures used to support claims in product labeling
- Enhance comparability/consistency of endpoints across clinical trial
- Improve efficiency for sponsors in endpoint selection
- Improve product labeling

# Initial Working Group Stages

## Scoping Stage

*FDA to review Scoping Stage Summary Document*

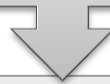


Vendor Selection Stage (prepare/release RFP, proposal review, & vendor selection)



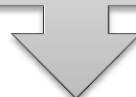
## Qualitative Research Stage

*FDA reviews Qualitative Research Summary Document*



## Quantitative Research Stage

*FDA reviews Quantitative Research Summary Document in draft "Qualification Dossier"*



## Qualification Stage

*FDA to review "Qualification Dossier" and make "fit-for-purpose" determination*

# Milestone Documents

## *Scoping Stage Summary Document:*

- PRO concept identification
- Proposed: target population, conceptual framework, claim, and endpoint model

## *Qualitative Research Summary Document:*

- Evidence for content validity of draft PRO measure including confirmation or revision of conceptual framework

# Milestone Documents

## *Quantitative Research Summary Document:*

- Evidence supporting measurement model and other measurement properties (i.e., reliability, construct validity, responsiveness) of final PRO instrument

## *Qualification Dossier:*

- Upon successful completion of the previous steps, the summary documents are combined into a “qualification dossier” that is submitted to the FDA

# Reasons for Reconsidering Stages

The *Qualitative Research Stage* provided evidence that the right content was identified and that items were selected/developed to capture that content; however, no quantitative item analysis was performed to provide evidence that the content was being adequately measured.

# Reasons for Reconsidering Stages

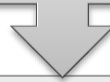
The *Qualitative Research Stage* did not provide evidence that:

- proposed multi-item scales are unidimensional
- all items are providing unique information
- the full range of item response options are used by respondents
- there are no floor or ceiling effects
- the proposed scoring scheme functions properly

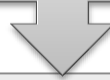
# Evolving Working Group Stages

## Scoping Stage

*FDA to review Scoping Stage Summary Document*



**Vendor Selection Stage (prepare/release RFP, proposal review, & vendor selection)**



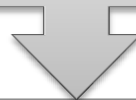
## Content Validity Stage

*FDA reviews Content Validity Summary Document*



## Psychometric Analysis Stage

*FDA reviews Psychometric Analysis Summary Document*



## Qualification Stage

*FDA to review "Qualification Dossier" and make "fit-for-purpose" determination*

# Continued Evolution

- The FDA's SEALD team is preparing a white paper delineating the questions they believe need to be answered to document content validity
- The PRO Consortium has convened a consultant panel to respond to the white paper and describe methodological and statistical approaches that can be used to answer the FDA's questions



# Conclusions

- This issue is far from settled within the PRO Consortium and beyond
- The right mix of qualitative and quantitative research during the Content Validity Stage remains an open question
- Whatever the outcome, decisions need to be driven by science and informed by pragmatism