Irritable Bowel Syndrome Working Group
Presented at the Third Annual PRO Consortium Workshop – Silver Spring, MD – April 4, 2012

Background

Rationale for Irritable Bowel Syndrome (IBS) Working Group (WG)
- PRO Consortium member representatives and FDA advisors identified IBS as a priority area.
- IBS lacks a standard and fit for purpose PRO instrument for measuring important patient-experienced aspects of IBS.
- There is a lack of a PRO instrument developed in accordance with the FDA PRO Guidance for use in clinical trials.

Goal of the IBS WG
- To develop PRO measures for patient-experienced symptoms in IBS for use in clinical trials as a primary endpoint to establish treatment benefit.

Targeted Labeling Language
- Treatment with product [X] results in an improvement in the symptoms of IBS-diarrhea-predominant, constipation-predominant, or mixed/alternating pattern, and diarrhea-predominant.
- This indication would have to be supported by an improvement in both abdominal symptoms and bowel movement-related symptoms as described in our conceptual framework.

Content of Interest

Endpoint Model for Treatment of IBS

- **Endpoint Hierarchy**: Primary, Related
- **Endpoint Concept(s)**: Relief of IBS symptoms
- **Clinical Outcome Assessment (COA)/Biomarker/Survival**: PRO

**Target Population**
- US-based adult patients (18 years and older; males and non-pregnant females)
- Diagnosis of IBS of all subtypes based on Rome III criteria (i.e., constipation-predominant, mixed or alternating pattern, and diarrhea-predominant)
- Patients without known or suspected organic disorder (e.g., Crohn's disease)
- Patients not concomitantly using medications known to affect GI mobility, constipation, or other IBS symptoms

**Hypothesized Conceptual Framework**

- **Abdominal Symptoms**
  - Abdominal Pain
  - Abdominal Discomfort
  - Abdominal Cramping
- **Bowel Movement-Related Symptoms**
  - stool consistency
  - stool frequency
  - incomplete BMs
  - recurrent BMs
  - urgency
  - straining

**Updates**
- RTI Health Solutions (RTI-HS) has completed the concept elicitation interviews and delivered final Concept Elicitation Report.
- Draft PRO instruments have been created for IBS-C (constipation-predominant) and IBS-D (diarrhea-predominant) and RTI-HS is currently cognitively debriefing the draft PRO instruments.
- Planning for pilot testing of draft instrument and need to select an ePRO vendor.

**Working Group Plans**

- **Next Steps**
  - To collaborate with the ePRO Consortium to implement the draft instruments onto an electronic data capture device.

- **Dissemination Plan**
  - To be developed through discussion and agreement between the IBS WG and RTI-HS.

**Topics for Discussion**

- **Concerns Worth Noting**
  - Bi-weekly teleconferences may not afford sufficient time for discussion and decision making among the WG members.
  - The approach to the measurement of symptoms in the IBS-mixed/alternating patient population has yet to be fully addressed.

- **Way in Which the Process Might Be Made More Efficient**
  - Collaboration among KOLs, IBS WG members, and the vendor is critical to the development process of the PRO measure.
  - Giving sponsors an opportunity to observe patient interviews is very helpful and fosters communication, clarity and smooth progression of the WG operations.

**Unique Issues for the Working Group and the Resolutions**

- The complexity of defining the relevant concepts and subtypes of IBS (IBS – constipation, and IBS – diarrhea).
- Through continued communication among the FDA representatives and IBS WG members, it was agreed to develop two IBS PRO measures (IBS-C and IBS-D), and the qualitative phase of content validation informed clarity of a range of complex concepts.

**Lessons learned**

- Collaboration among KOLs, IBS WG members, and the vendor is critical to the development process of the PRO measure.
- Giving sponsors an opportunity to observe patient interviews is very helpful and fosters communication, clarity and smooth progression of the WG operations.

**Working Group Participants**

- **Company/Organization**
  - Ironwood Pharmaceuticals, Inc.
  - Forest Research Institute
  - Takeda Pharmaceuticals International

- **Name**
  - Mollie Baird, MPH (Co-Chair); Jeff Johnston, MD
  - Robyn T. Carson, MPH; Steven J. Stiff, MD
  - Charles Baum, MD (Co-Chair)

- **Nonmember Participants**
  - Nancy Norton, BS
  - Lin Chang, MD
  - Brennan M.R. Spiegel, MD, MSHS
  - Jeffrey M. Lackner, PhD

- **Affiliation**
  - International Foundation for Functional Gastrointestinal Disorders (IFFGD)
  - University of California, Los Angeles
  - University of California, Los Angeles
  - University at Buffalo, SUNY

- **Expert Panel Members**
  - William D. Chey, MD
  - Douglas A. Drossman, MD
  - Mark P. Jensen, PhD

- **Affiliation**
  - University of Michigan
  - University of North Carolina, Chapel Hill
  - University of Washington

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<tr>
<th>Milestone</th>
<th>Expected Date</th>
<th>Completed Date</th>
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<tr>
<td>Scoping Stage</td>
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<tr>
<td>Content Validity Stage</td>
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<td>Vendor selection and contracting</td>
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<td>Completion of background research (literature review and 1st expert panel)</td>
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<td>Refining initial instrument (cognitive interviewing, final expert panel, identification of electronic data capture (ePRO) platform, translatability assessment)</td>
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<td>Quantitative analysis</td>
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<td>Content Validity Summary document submitted to FDA for interim review</td>
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**Expert Panel**

- **Research Team**
  - Shari Fehnel, PhD; Claire Ervin, MPH; Diana Lin Chang, MD; Brennan M.R. Spiegel, MD, MSHS; William D. Chey, MD; Douglas A. Drossman, MD; Mark P. Jensen, PhD; Charles Baum, MD (Co-Chair); Mollie Baird, MPH (Co-Chair); Jeff Johnston, MD.

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**Contract Research Organization**

- RTI Health Solutions
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