# Functional Dyspepsia Working Group

## Presented at the Seventh Annual PRO Consortium Workshop – Silver Spring, MD – April 27-28, 2016

PRO CONSORTIUM CRITICAL PATH INSTITUTE

## Background

### Rationale for Functional Dyspepsia (FD) Working Group (WG)

- PRO Consortium member representatives and FDA advisors identified FD as an area lacking a "well-defined and reliable" measure of treatment benefit

### Goal of the FD WG

- To develop a PRO instrument, in accordance with the FDA PRO Guidance, to assess the symptoms of FD for use in clinical trials as a primary endpoint measure to establish treatment benefit

### Targeted Labeling Language

- The PRO measure would support an indication for the treatment of the FD subtype as defined by the Rome III diagnostic criteria:
  1) Postprandial distress syndrome (PDS), which includes symptoms such as postprandial fullness and early satiation;
  2) Epigastric pain syndrome (EPS), which involves symptoms such as epigastric pain and burning; or
  3) Co-existing PDS and EPS subtypes

## Milestones

| Milestone | Expected Date | Completed Date |
|---|---|---|
| Content Validity Stage | | |
| Vendor selection and contracting | | September 18, 2012 |
| Complete background research (Literature Review Report and Expert Panel input) | | August 30, 2013 |
| Submit Literature Review & Concept Elicitation Protocol to FDA for consultation and advice | | October 31, 2013 |
| Received written comments from the FDA | | December 20, 2013 |
| Submitted working group's responses to FDA comments | | February 7, 2014 |
| Complete initial concept elicitation interviews and generate items (concept elicitation interviews, item generation, expert panel input) | | March 2, 2015 |
| Complete translatability and ePRO implementation assessments | | April 2015 |
| Complete cognitive interviews and revise instrument | 4Q2016 | |
| Submit Qualitative Research Summary Briefing Document to FDA for review and feedback | 1Q2017 | |
| Complete documentation of content validity and cross-sectional evaluation of other measurement properties | TBD | |
| Submit exploratory endpoint qualification dossier to FDA | TBD | |

## Highlights

**Example Endpoint model for treatment of FD – Postprandial Distress Syndrome (PDS) Subtype**

| x | Concept(s) | Endpoint Type |
|---|---|---|
| Primary | FD-PDS Subtype<br>• PDS Symptoms Score | PRO instrument under development |

**Example Endpoint model for treatment of FD – Epigastric Pain Syndrome (EPS) Subtype**

| Endpoint Hierarchy | Concept(s) | Endpoint Type |
|---|---|---|
| Primary | FD-EPS Subtype<br>• EPS Symptom Score | PRO instrument under development |

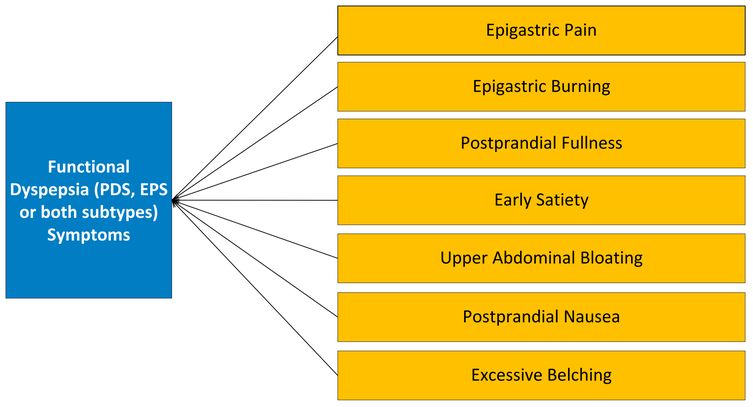
**Example Endpoint model for treatment of FD – Co-existing PDS and EPS symptoms**

| Endpoint Hierarchy | Concept(s) | Endpoint Type |
|---|---|---|
| Primary | FD<br>• PDS and EPS Symptoms Score | PRO instrument under development |

### Target Population

- U.S. adult patients aged 18 years and older, with a diagnosis of FD (including PDS, EPS, or both) according to the Rome III diagnostic criteria, inclusive of a recent negative endoscopy
- Exclusion criteria include the following conditions: patients with gastroparesis, active irritable bowel syndrome, active chronic constipation, and active GERD (list not exhaustive)

### Hypothesized Conceptual Framework




## Updates

- Obtained additional guidance on inclusion and exclusion criteria for cognitive interviews from FDA's Qualification Review Team (QRT)
- Cognitive interviews were initiated and are ongoing
- Selected Biomedical Systems for implementation of the *Functional Dyspepsia Symptom Diary (FDSD)* on a handheld device for preliminary quantitative data collection and item analysis

## Working Group Plans

### Information Dissemination Update

- Taylor F, et al. Development of a Symptom-based Patient-reported Outcome Instrument for Functional Dyspepsia: A Preliminary Conceptual Model and an Evaluation of the Adequacy of Existing Instruments. *The Patient - Patient-Centered Outcomes Research*, In press (Published online March 28, 2016) – open access
- Second manuscript will focus on the qualitative research

### Next Steps

- Complete cognitive interviews , draft report of cognitive interview findings, and update *FDSD*
- Continue to investigate through quantitative research whether there are two individual subtypes of FD (EPS and PDS)
- Develop the qualitative research summary document and corresponding manuscript

## Topics for Discussion

### Unique Issues for the Working Group

- Recruitment challenges encountered in identifying patients with FD diagnosis that do not have other co-existing GI disorders
  - Very extensive list of exclusion criteria from FDA, further complicated by potential discrepancy between clinician-reported and patient-reported symptoms
  - Compromise reached with the FDA's QRT to allow enrollment of patients with comorbid conditions with future evaluation planned regarding the impact of these comorbid conditions on the patients' FD-symptom experience
- Challenge articulating concepts when developing several key items (i.e., early satiety and burping/belching)
  - Item wording will be tested in cognitive interviews

### Lessons Learned

- Do not assume an accepted definition of condition exists
- Do not assume that certain terminology is universally understood (e.g., conceptual framework and conceptual model)
- When possible, consult recruiting agencies and clinical sites to assess feasibility of inclusion/exclusion criteria before finalizing
- Despite FDA's interest for having the instrument development sample free of confounding conditions (i.e., a "pure-FD" sample), it is critical that the sample represents the real-world FD population to ensure that future research is feasible and relevant

## Working Group Participants

| Organization | Name |
|---|---|
| Allergan | Robyn Carson, MPH (Co-Chair); Steven J. Shiff, MD |
| Ironwood Pharmaceuticals, Inc. | David Reasner, PhD (Co-Chair); Jennifer Hanlon, MPH |
| **Expert Panel Members** | **Affiliation** |
| Brian E. Lacy, MD, PhD | Dartmouth-Hitchcock Medical Center |
| Henry P. Parkman, MD | Temple University |
| Jan Tack, MD | University of Leuven |
| Nick Talley, MD, PhD | University of Newcastle |

| Contract Research Organization | Research Team |
|---|---|
| Adelphi Values | Alan Shields, PhD; Fiona Taylor, MBiochem; Catherine Foley, MPH, MA; Megan Daggett, BA; Sophie Higgins, MPH |
| **ePRO System Provider** | **Representative** |
| Biomedical Systems | Serge Bodart, MS |