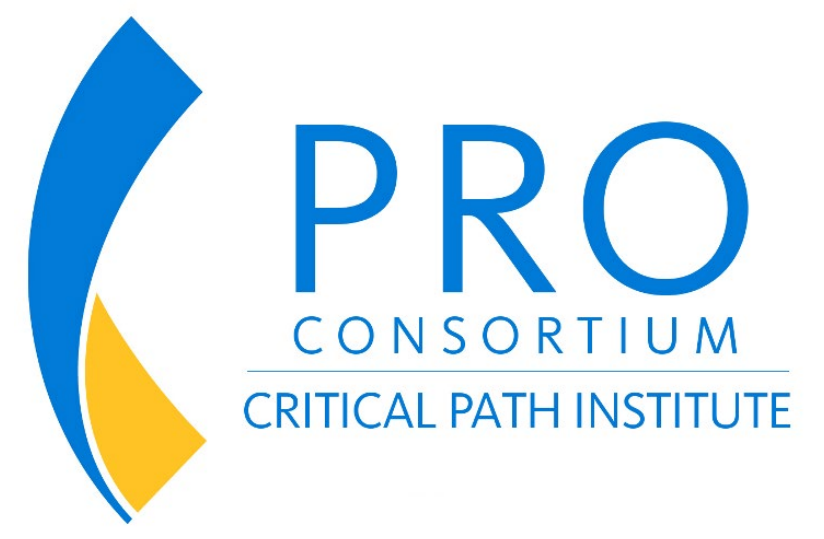


# Functional Dyspepsia Working Group

14<sup>th</sup> Annual PRO Consortium Workshop – Silver Spring, MD – April 19-20, 2023



## 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 clinical benefit

### Goal of the FD WG

- To develop a PRO measure to assess the symptoms of FD for use in clinical trials as a primary endpoint measure to establish clinical benefit

### Targeted Labeling Language

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

## Milestones

Milestone	Expected Date	Completed Date
Letter of Intent submission to FDA		JUN 2010
Accepted into the COA Qualification Program		FEB 2012
Literature Review and Concept Elicitation Protocol submission to FDA		OCT 2013
Received written comments from the FDA		DEC 2013
Submitted working group’s responses to FDA comments		FEB 2014
Qualification Briefing Package submission for <i>Functional Dyspepsia Symptom Diary (FDSD)</i> to FDA		NOV 2017
FDA response received that further evidence was needed		JAN 2019
Meeting with QRT to path forward		JUL 2019
Qualification Plan submission for <i>FDSD</i> to FDA		AUG 2020
Received Qualification Plan Determination Letter from FDA		APR 2022
Full Qualification Package submission for <i>FDSD</i> to FDA	TBD	

## Highlights

### Example Endpoint Model for Treatment of FD – Postprandial Distress Syndrome (PDS) Subtype

Endpoint Hierarchy	Concept(s)	Endpoint Type
Primary	Total Symptom Score (stomach burning, stomach pain, bloating, postprandial fullness, early satiety)	PRO ( <i>FDSD</i> )

### Example Endpoint Model for Treatment of FD – Epigastric Pain Syndrome (EPS) Subtype

Endpoint Hierarchy	Concept(s)	Endpoint Type
Primary	Total Symptom Score (stomach burning, stomach pain, bloating, postprandial fullness, early satiety)	PRO ( <i>FDSD</i> )

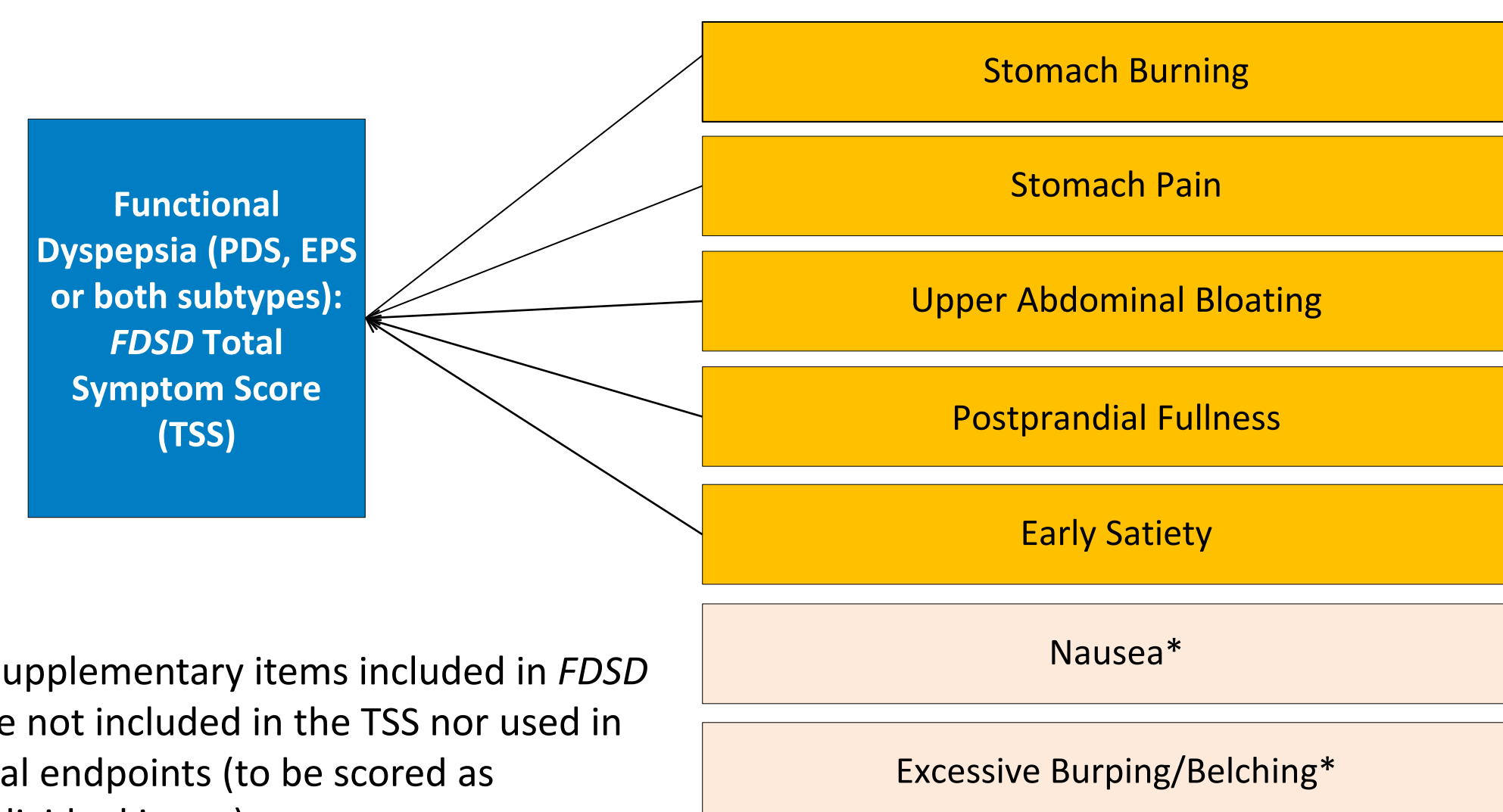
### Example Endpoint Model for Treatment of FD – Co-existing PDS and EPS Symptoms

Endpoint Hierarchy	Concept(s)	Endpoint Type
Primary	Total Symptom Score (stomach burning, stomach pain, bloating, postprandial fullness, early satiety)	PRO ( <i>FDSD</i> )

### 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 IV 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)

### Conceptual Framework



\*Supplementary items included in *FDSD* are not included in the TSS nor used in trial endpoints (to be scored as individual items)

### Measure – *Functional Dyspepsia Symptom Diary (FDSD)*

- Core items:** Five core symptom domains plus two supplementary domains
- Recall Period:** Past 24 hours
- Response Options:** 11-point numeric rating scale
- Symptom Attribute:** Severity was chosen based on patient descriptions of FD symptom experience
- Data Collection Mode:** Smartphone-type device used during cognitive interviews

## Working Group Activities

### Completed Activities

- FDSD* Qualification Briefing Package submitted to FDA in November 2017. Further evidence requested in FDA response in February 2019.
- Qualification Plan submitted to FDA in August 2020 and accepted by FDA in April 2022.

### Information Dissemination

- 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* 2016;9:409-418
- Presentation at 2016 American Gastroenterology Association (AGA) Drug Development Conference: Clinical Endpoints in Upper GI Disorders and endorsement in their white paper
- Taylor F et al. Development of a symptom-focused patient-reported outcome measure for functional dyspepsia: the *Functional Dyspepsia Symptom Diary (FDSD)*. *Am J Gastroenterol.* 2018;113(1):39-48 (in first ever AJG issue focused on “Putting Patients First”)

### Unique Issues for the Working Group

- Recruitment challenges encountered in identifying participants with FD diagnosis without other co-existing gastrointestinal (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 Qualification Review Team to allow enrollment of participants with comorbid conditions for cognitive interviews with evaluation 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 was successfully tested in cognitive interviews

### Lessons Learned

- Do not assume an accepted definition of condition exists and 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 protocol
- Despite FDA’s interest in having the measure 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

Company/Organization	Representatives
AbbVie	Robyn T. Carson, MPH (Co-Chair)
Ironwood Pharmaceuticals, Inc.	Douglas Taylor, MBA (Co-Chair)
Expert Panel Members	Affiliation
Brian E. Lacy, MD, PhD	Mayo Clinic
Henry P. Parkman, MD	Temple University
Jan Tack, MD, PhD	University of Leuven
Nicholas Talley, MD, PhD	University of Newcastle
Research Partner	Research Team
Adelphi Values	Alan Shields, PhD; Fiona Taylor, MBiochem; Catherine Foley, MPH, MA; Sophie Higgins, MPH; Emily Brennan, MPH; Megan Daggett, BA (at time of study)
ePRO System Provider	Representative
Biomedical Systems	Serge Bodart, MS (at time of study)