Welcome to Ninth Annual Patient-Reported Outcome Consortium Workshop

April 25 – 26, 2018 ■ Silver Spring, MD

Network: Cypress-Guest ; Passcode: Cyp24689

Welcome and PRO Consortium Update

Stephen Joel Coons, PhD
Executive Director, PRO Consortium

Ninth Annual
Patient-Reported Outcome Consortium Workshop

April 25 – 26, 2018 ■ Silver Spring, MD

CRITICAL PATH INSTITUTE
collaborate · innovate · accelerate

Workshop Packet Contents

- Welcome Letter
- Workshop Agenda
- PRO Consortium Fact Sheet
- Presenters and Panelists Biographical Sketches
- Pre-Registrant List
- **Workshop Feedback Form**

Acknowledgments

Critical Path Institute and the PRO Consortium are supported in part by grant U18 FD005320 (effective 2015-2020) from the U.S. Food and Drug Administration.

Disclaimer

- The views and opinions expressed in the following slides are those of the individual presenters and should not be attributed to their respective organizations/companies, the U.S. Food and Drug Administration, or the Critical Path Institute.

-

Patient-Reported Outcome (PRO) Consortium

- Formed in late 2008 by C-Path in cooperation with FDA's Center for Drug Evaluation and Research (CDER) and the pharmaceutical industry

- Membership
  - 24 members (pharmaceutical firms)

- Additional Participants
  - Representatives of governmental agencies (FDA, NIH)
  - Clinical consultants, patients, academic researchers, and contract research organizations partnering in the development of PRO measures and other clinical outcome assessment (COA) tools

PRO Consortium Members

abbvie

ALLERGAN

AMGEN

AstraZeneca

AVROBIO

BAYER

Boehringer Ingelheim

Bristol-Myers Squibb

cti BIOPHARMA

Daiichi-Sankyo

EMD SERONO

gsk GlaxoSmithKline

Genentech
A Member of the Roche Group

Ironwood

Johnson & Johnson

Lilly

MERCK

NOVARTIS

Pfizer

SANOFI

Shire

SUNOVION

Takeda

ucb

PRO Consortium Mission

To establish and maintain a collaborative framework with appropriate stakeholders for the qualification of patient-reported outcome (PRO) instruments and other clinical outcome assessment (COA) tools that will be publicly available for use in clinical trials **where COA-based endpoints are used to support product labeling claims**

PRO Consortium Goals

- Enable pre-competitive collaboration that includes FDA input and expertise
- Obtain FDA qualification of PRO measures and other COA tools for use in assessing primary or secondary clinical trial endpoints
- Avoid development of multiple endpoint measures for the same purpose
- Share costs of developing new endpoint measures
- Facilitate FDA's review of medical products by standardizing COA-based endpoint measures that will be publicly available

Current Working Groups/Number of Funding Firms

PRO CONSORTIUM
CRITICAL PATH INSTITUTE

▪ Asthma	10 member firms
▪ Cognition	9 member firms
▪ Depression	8 member firms
▪ Functional Dyspepsia	3 member firms
▪ Irritable Bowel Syndrome (IBS)	3 member firms
▪ Multiple Sclerosis (MS)	6 member firms
▪ Myelofibrosis	2 member firms
▪ Non-Small Lung Cancer (NSCLC)	11 member firms
▪ Pediatric Asthma	3 member firms
▪ Rheumatoid Arthritis (RA)	5 member firms

Goal of Working Groups

To produce and/or compile the necessary evidence to enable new or existing COAs to be qualified by the FDA for use in clinical trials where COA-based endpoints can be used to support product labeling claims.

Working Group Updates

During Workshop breaks, please view the working group posters at the back of the meeting room.

The posters will also be on display during the reception in Cedar (First Floor) from 5:30 pm – 7:00 pm this evening.

Asthma Working Group

Co-Chairs: TBD - Linda Nelsen (GlaxoSmithKline), immediate past chair

Target population: Adults and adolescents with a clinical diagnosis of mild to severe persistent asthma

Measurement concept: Daytime and nighttime asthma symptoms

Role in endpoint hierarchy: Co-primary or secondary endpoint measure to establish or support treatment benefit

Name of PRO measure: *Asthma Daily Symptom Diary* (*ADSD*)

Status: Revised *ADSD* Qualification Briefing Package to be submitted to FDA in 2018 Q2

Cognition Working Group

Co-Chairs: Scott Andrews (Eli Lilly and Company) and Katy Benjamin (AbbVie)

Target population: Adults with a clinical diagnosis of mild cognitive impairment (MCI) due to Alzheimer's disease

Measurement concept: day-to-day functioning

Role in endpoint hierarchy: Primary or co-primary endpoint measure to establish treatment benefit

Name of PerfO measure: *University of California San Diego Performance-based Skills Assessment* (*UPSA*)

Status: Conducting foundational work to support development of an Initial Briefing Package

Depression Working Group

Co-Chairs: Nicki Bush (Eli Lilly and Company) and Lucy Abraham (Pfizer, Inc.)

Target population: Adults with a clinical diagnosis of major depressive disorder

Measurement concept: Symptoms of major depressive disorder

Role in endpoint hierarchy: Primary or secondary endpoint measure to establish or support treatment benefit

Name of PRO measure: *Symptoms of Major Depressive Disorder Scale* (*SMDDS*)

Status: ***SMDDS*** **was qualified by FDA for exploratory use in November 2017**

Qualification of Symptoms of Major Depressive Disorder Scale, a Patient-Reported Outcome Instrument for Measurement of Symptoms of Major Depressive Disorder

Date: November 27, 2017

DDT Type: Clinical outcome assessment (COA)

DDT Tracking Number: DDTCOA-00008

Referenced COA: Symptoms of Major Depressive Disorder Scale (SMDDS)

Type of COA: Patient-Reported Outcome (PRO) Instrument

The Center for Drug Evaluation and Research has determined that the SMDDS is qualified for exploratory use to measure symptoms of major depressive disorder (MDD) in the context of use described below.

Full qualification statement available at:
https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm450689.htm

Functional Dyspepsia Working Group

Co-Chairs: Robyn Carson (Allergan) and David Reasner (Ironwood)

Target population: Adults with a clinical diagnosis of functional dyspepsia

Measurement concept: Functional dyspepsia symptom severity

Role in endpoint hierarchy: Primary endpoint measure to establish treatment benefit

Name of PRO measure: *Functional Dyspepsia Symptom Diary* (*FDSD*)

Status: *FDSD* Qualification Briefing Package submitted to FDA on November 14, 2018

Development of a Symptom-Focused Patient-Reported Outcome Measure for Functional Dyspepsia: The Functional Dyspepsia Symptom Diary (FDSD)

Fiona Taylor MBiochem, Sophie Higgins MPH, Robyn T Carson MPH, Sonya Eremenco MA, Catherine Foley MPH, MA, Brian E Lacy MD, PhD, Henry P Parkman MD, David S Reasner PhD, Alan L Shields PhD, Jan Tack MD, PhD & Nicholas J Talley MD, PhD on behalf of the Patient-Reported Outcome Consortium's Functional Dyspepsia Working Group

The American Journal of Gastroenterology **113**, 39–48 (2018)

doi:10.1038/ajg.2017.265

Received: 02 April 2017

Accepted: 01 July 2017

Published: 19 September 2017

IBS Working Group

Co-Chairs: Robyn Carson (Allergan) and Jennifer Hanlon (Ironwood)

Target population: Adults with a diagnosis of IBS, including three main subtypes: IBS-C (constipation predominant), IBS-D (diarrhea predominant) and IBS-M (mixed)

Measurement concepts: Abdominal and bowel movement-related symptoms

Role in endpoint hierarchy: Primary endpoint measure to establish treatment benefit

Name of measures: *Diary for Irritable Bowel Syndrome Symptoms – Constipation (DIBSS-C), DIBSS-D*, and *DIBSS-M*

Status: Target for *DIBSS-C* qualification submission is mid-late 2018, with the others to follow

Multiple Sclerosis Working Group

Co-Chairs: TBD

Target population: Adults with a clinical diagnosis of multiple sclerosis (MS)

Measurement concepts: Symptom severity and functional impact

Role in endpoint hierarchy: Secondary endpoint measures supporting treatment benefit

Name of proposed PRO measures: PROMIS® short forms proposed to assess fatigue and physical function in patients with all forms of MS

Status: Initial Briefing Packages to be prepared, augmented by qualitative research contributed to the working group by Merck KGaA

Myelofibrosis Working Group

Co-Chairs: TBD

Target population: Adults aged 18 years and older with a clinical diagnosis of myelofibrosis

Measurement concept: Myelofibrosis symptom severity

Role in endpoint hierarchy: Secondary endpoint measure supporting treatment benefit

Name of measure: *Myelofibrosis Symptom Assessment Form (MFSAF) v4.0*

Status: Considering submission for qualification for exploratory use

NSCLC Working Group

Co-Chairs: Astra Liepa (Eli Lilly and Company) and Tom Karagiannis (Genentech)

Target population: Adult patients with advanced NSCLC (stages IIIb/IV and ECOG performance status of 0-2)

Measurement concept: NSCLC symptom severity

Role in endpoint hierarchy: Secondary endpoint measure to support treatment benefit

Name of PRO measure: *Non-Small Cell Lung Cancer Symptom Assessment Questionnaire* (*NSCLC-SAQ*)

Status: ***NSCLC-SAQ*** **was qualified by FDA for exploratory use in April 2018**

Qualification of Non-Small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ) – A Patient-Reported Outcome Instrument

Date: April 4, 2018

DDT Type: Clinical Outcome Assessment (COA)

DDT Tracking Number: DDTCOA-00009

Referenced COA: Non-Small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ)

Type of COA: Patient-Reported Outcome (PRO) Instrument

The Center for Drug Evaluation and Research (CDER) has determined that the NSCLC-SAQ is qualified for exploratory use to measure symptoms of non-small cell lung cancer (NSCLC) in the context of use described below. Sponsors should engage the review division early and throughout drug development to discuss the use of NSCLC-SAQ to support labeling claims for their drug development programs.

Full qualification statement for NSCLC available at:
https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm450689.htm

Pediatric Asthma Working Group

Co-Chairs: TBD

Target population: Children 4 to 11 years old with a clinical diagnosis of mild to severe persistent asthma requiring a daily long-term control medication

Measurement concepts: Pediatric asthma symptoms

Role in endpoint hierarchy: Co-primary or secondary endpoint measure supporting daytime and night-time treatment benefit

Name of COA measure: TBD

Status: Initial Briefing Package to be prepared based on FDA feedback received January 2018, incorporating Merck's ObsRO diary to be used for entire age range (4 to 11 years of age) and self-report (PRO diary) by children (8 to 11 years of age)

Rheumatoid Arthritis Working Group

Co-Chairs: April Naegeli (Eli Lilly and Company) and Enkeleida Nikai (Eli Lilly and Company)

Target population: Adults with a clinical diagnosis of mild to severe rheumatoid arthritis

Measurement concept: Rheumatoid arthritis-related fatigue

Role in endpoint hierarchy: Secondary endpoint measure supporting treatment benefit

Name of PRO Measure: *PROMIS® – Short Form Fatigue 10a*

Status: Developing Qualification Plan

Since Last Year's Workshop…

Two Letters of Intent accepted by FDA's COA qualification program

- Pediatric Asthma WG
- Multiple Sclerosis WG

One Initial Briefing Package submitted to FDA:

- Rheumatoid Arthritis WG

One Qualification Briefing Package submitted to FDA:

- Functional Dyspepsia WG – *Functional Dyspepsia Symptom Diary (FDSD)*

Two measures qualified by FDA:

- *Symptoms of Major Depressive Disorder Scale* (*SMMDS*)
- *Non-small Cell Lung Cancer Symptom Assessment Questionnaire* (*NSCLC-SAQ*)

Since Last Year's Workshop…

PRO Consortium-developed measures were being used in member firms' clinical trials (pre-qualification):

- *Asthma Daily Symptom Diary (ADSD)*
- *Diary for Irritable Bowel Syndrome Symptoms – Constipation (DIBSS-C)*
- *Myelofibrosis Symptom Assessment Form (MFSAF) v4.0*
- *Non-Small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ)*
- *Symptoms of Major Depressive Disorder Scale (SMDDS)*

Since Last Year's Workshop…

In addition to the qualifications….

- Multiple presentations at international scientific/clinical meetings were provided based on PRO Consortium working group research
- A PRO Consortium instrument translation process was developed through a consensus development initiative involving translation companies and member firms
- Held (in conjunction with the ePRO Consortium) a Critical Path Innovation Meeting with FDA to address the use of wearable devices to collect efficacy endpoint data in clinical trials

Since Last Year's Workshop…

- Eremenco S, Pease S, Mann S, Berry P and on behalf of the PRO Consortium's Process Subcommittee. Patient-Reported Outcome (PRO) Consortium translation process: consensus development of updated best practices. *Journal of Patient Reported Outcomes* (2018) 2:12. https://doi.org/10.1186/s41687-018-0037-6.
- Acquadro C, Patrick DL, Eremenco S, Martin ML, Kulis D, Correia H, Conway K and on behalf of the International Society of Quality of Life Research (ISOQOL) Translation and Cultural Adaptation Special Interest Group TCA-SIG). Emerging good practices for translatability assessment (TA) of patient-reported outcome (PRO) measures. *Journal of Patient Reported Outcomes* (2018) 2: 8. https://doi.org/10.1186/s41687-018-0035-8.
- Byrom B, Watson C, Doll H, Coons SJ, Eremenco S, Ballinger R, McCarthy M, Crescioni M, O'Donohoe P, Howry C. Selection of and evidentiary considerations for wearable devices and their measurements for use in regulatory decision making: recommendations from the ePRO Consortium. *Value in Health*. In press. (Published online: November 7, 2017) https://doi.org/10.1016/j.jval.2017.09.009.
- Kluetz PG, Kanapuru B, Lemery S, et al. Informing the tolerability of cancer treatments using patient-reported outcome (PRO) measures: summary of an FDA and Critical Path Institute workshop. *Value in Health*. In press (Published online: November 7, 2017) https://doi.org/10.1016/j.jval.2017.09.012.

Active Participation During the Q&A Portion of Each Session is Encouraged

Before you speak, please go to the microphone or wait until a microphone is handed to you

The workshop is being audio recorded

Please turn off cell phones or set to vibrate

FDA Annual Update

- Michelle Campbell, PhD, Reviewer and Scientific Coordinator, COA Staff, OND