Welcome to Eighth Annual Patient-Reported Outcome Consortium Workshop

April 26 – 27, 2017 ■ Bethesda, MD

Wireless: @Hyatt Meeting; Passcode: COA2017

Welcome and PRO Consortium Update

Stephen Joel Coons, PhD
Executive Director, PRO Consortium

Eighth Annual
Patient-Reported Outcome Consortium Workshop

April 26 – 27, 2017 ■ Bethesda, MD

CRITICAL PATH INSTITUTE
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Workshop Packet Contents

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Acknowledgments

Critical Path Institute and the PRO Consortium are supported by grant 1U18FD005320 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.

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Patient-Reported Outcome (PRO) Consortium

PRO CONSORTIUM
CRITICAL PATH INSTITUTE

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

- Membership
  - 26 members (pharmaceutical firms)

- Non-Voting 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

ACTELION

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

HORIZON PHARMA

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 (WG)

PRO CONSORTIUM
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▪ Asthma	10 member firms
▪ Cognition	9 member firms
▪ Depression	9 member firms
▪ Functional Dyspepsia	2 member firms
▪ Irritable Bowel Syndrome (IBS)	3 member firms
▪ Multiple Sclerosis (MS)	5 member firms
▪ Myelofibrosis	2 member firms
▪ Non-Small Lung Cancer (NSCLC)	10 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 clinical outcome assessment (COA) tools to be qualified by the FDA for use in clinical trials where COA endpoints can be used to support product labeling claims.

* Myelofibrosis WG is the one exception

Working Group Updates

During Workshop breaks, please view the working group posters outside the meeting room.

The posters will also be on display during the reception on the Terrace from 5:30 pm – 7:00 pm this evening.

Asthma Working Group

Co-Chairs: Linda Nelsen (GlaxoSmithKline LLC) and TBD

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 to establish or support treatment benefit

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

Status: ***ADSD* Qualification Briefing Package submitted to FDA on December 22, 2016**

VALUE IN HEALTH 19 (2016) 440–450

Available online at www.sciencedirect.com

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Patient-Reported Outcome

Assessing Asthma Symptoms in Adolescents and Adults: Qualitative Research Supporting Development of the Asthma Daily Symptom Diary

Adam Gater, MSc[1,], Linda Nelsen, MHS[2], Sarah Fleming, MPH[3], J. Jason Lundy, PhD[4], Nicola Bonner, MSc[1], Rebecca Hall, MMedSci[1], Chris Marshall, MSc[1], Hannah Staunton, MSc[1], Jerry A. Krishnan, MD, PhD[5], Stuart Stoloff, MD[6], Michael Schatz, MD[7], John Haughney, MD[8], on behalf of the Patient-Reported Outcome Consortium's Asthma Working Group*

[1]*Adelphi Values Ltd., Adelphi Mill, Bollington, Cheshire, UK;* [2]*GlaxoSmithKline, King of Prussia, PA, USA;* [3]*Janssen Global Services LLC, Titusville, NJ, USA;* [4]*Outcometrix, Tucson, AZ, USA;* [5]*University of Illinois Hospital and Health Sciences System, Medical Center Administration, Chicago, IL, USA;* [6]*University of Nevada, Reno, NV, USA;* [7]*Kaiser Permanente Medical Center/Kaiser Foundation Hospital, San Diego, CA, USA;* [8]*University of Aberdeen, King's College, Aberdeen, UK*

Cognition Working Group

Co-Chairs: Scott Andrews (Eli Lilly and Company) and Chris Edgar (Roche)

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 **c**o-primary endpoint to establish treatment benefit

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

Status: WG, in conjunction with the developer and other content experts, is evaluating the UPSA's tasks to ensure they (1) reflect contemporary aspects of day-to-day functioning and (2) will be cross-culturally relevant and adaptable for use in multinational trials

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 concepts: Symptoms of major depressive disorder

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

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

Status: ***SMDDS* Qualification Briefing Package submitted to FDA on March 28, 2017**

Functional Dyspepsia Working Group

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

Target population: Adults with a clinical diagnosis of functional dyspepsia

Measurement concepts: Symptoms of functional dyspepsia

Role in endpoint hierarchy: Primary endpoint to establish treatment benefit

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

Status: Qualitative research completed along with preliminary quantitative assessment of item and scale performance; Initial Briefing Package will be prepared and submitted by end of June 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 to establish treatment benefit

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

Status: All participants completed the Quantitative Pilot Study, but data collection device software problems were identified and additional data collection is likely to be necessary

VALUE IN HEALTH 20 (2017) 618–626

Available online at www.sciencedirect.com

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journal homepage: www.elsevier.com/locate/jval

Development of the Diary for Irritable Bowel Syndrome Symptoms to Assess Treatment Benefit in Clinical Trials: Foundational Qualitative Research

Sheri E. Fehnel, PhD[1,], Claire M. Ervin, MPH[1], Robyn T. Carson, MPH[2], Gianna Rigoni, PharmD, MS[3], Jeffrey M. Lackner, PsyD[4], Stephen Joel Coons, PhD[5], on behalf of the Critical Path Institute Patient-Reported Outcome Consortium's Irritable Bowel Syndrome Working Group*

[1]*RTI Health Solutions, Research Triangle Park, NC, USA;* [2]*Allergan plc, Jersey City, NJ, USA;* [3]*AstraZeneca, Wilmington, DE, USA;* [4]*University at Buffalo School of Medicine, SUNY, Buffalo, NY, USA;* [5]*Critical Path Institute, Tucson, AZ, USA*

Multiple Sclerosis Working Group

Co-Chairs: TBD

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

Measurement concepts: Symptom severity and functional impact

Role in endpoint hierarchy: Secondary endpoint supporting treatment benefit

Name of proposed PRO measures: PROMIS *Physical Function Short Form 10a* and Neuro-QOL *Ability to Participate in Social Roles and Activities – Short Form*

Status: Letter of Intent submitted to FDA on December 6, 2016

Myelofibrosis Working Group

Goal: Develop a harmonized myelofibrosis symptom questionnaire (including fatigue, night sweats, itching, abdominal discomfort, early satiety, pain under ribs on left side, and bone pain) for use as a secondary endpoint measure.

Milestone: Harmonization Panel Meeting held March 2, 2016, resulting in the *Myelofibrosis Symptom Assessment Form* (*MFSAF*) v4.0 (24-hour and 7-day)

Next steps:

- Manuscript titled "Development of a Harmonized Patient-Reported Outcome Questionnaire to Assess Myelofibrosis Symptoms in Clinical Trials" revised and resubmitted to *Leukemia Research*
- **The *MFSAF v4.0* (©Mayo Clinic) is publicly available for licensing through the PRO Consortium**

NSCLC Working Group

Co-Chairs: Astra Liepa (Eli Lilly and Company) and Kendra DeBusk (Genentech, Inc.)

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

Measurement concepts: Symptoms of NSCLC

Role in endpoint hierarchy: Secondary endpoint to support treatment benefit

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

Status: ***NSCLC-SAQ* Qualification Briefing Package submitted to FDA on March 30, 2017**

Original Research

Qualitative Development and Content Validity of the Non–small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ), A Patient-reported Outcome Instrument

Kelly P. McCarrier, PhD, MPH[1]; Thomas M. Atkinson, PhD[2]; Kendra P.A. DeBusk, PhD[3]; Astra M. Liepa, PharmD[4]; Michael Scanlon, MA[1]; Stephen Joel Coons, PhD[5]; and on behalf of the Patient-Reported Outcome Consortium, Non–Small Cell Lung Cancer Working Group[†]

[1]Health Research Associates, Mountlake Terrace, Washington; [2]Department of Psychiatry and Behavioral Sciences, Memorial Sloan Kettering Cancer Center, New York, New York; [3]Patient-Centered Outcomes Research, Genentech, South San Francisco, California; [4]Global Patient Outcomes and Real World Evidence, Eli Lilly and Company, Indianapolis, Indiana; and [5]Critical Path Institute, Patient-Reported Outcome Consortium, Tucson, Arizona

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: Secondary endpoint supporting daytime and night-time treatment benefit

Name of COA measure: TBD – co-completed (parent/caregiver and child) measure being proposed

Status: Letter of Intent submitted to FDA on December 2, 2016

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 supporting treatment benefit

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

Status: Preparing Initial Briefing Package for submission to FDA in May or June 2017

Since Last Year's Workshop…

Four letters of intent submitted to FDA:

- Cognition WG
- Rheumatoid Arthritis WG
- Multiple Sclerosis WG
- Pediatric Asthma WG

Three qualification briefing packages submitted to FDA (for exploratory use):

- Asthma WG – *Asthma Daily Symptom Diary* (*ADSD*)
- Depression WG – *Symptoms of Major Depressive Disorder Scale* (*SMMDS*)
- NSCLC WG – *Non-small Cell Lung Cancer Symptom Assessment Questionnaire* (*NSCLC-SAQ*)

Since Last Year's Workshop…

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

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

Since Last Year's Workshop…

Co-Sponsored with FDA:

Second Annual Workshop on Clinical Outcome Assessments in Cancer Clinical Trials on April 25, 2017, in Bethesda, MD

In addition to the previously mentioned published articles:

- 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
- The decision was made to partner with FACIT.org on the development of a licensing and distribution website for PRO Consortium instruments

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

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

The workshop is being audio recorded

Please turn off cell phones or set to vibrate