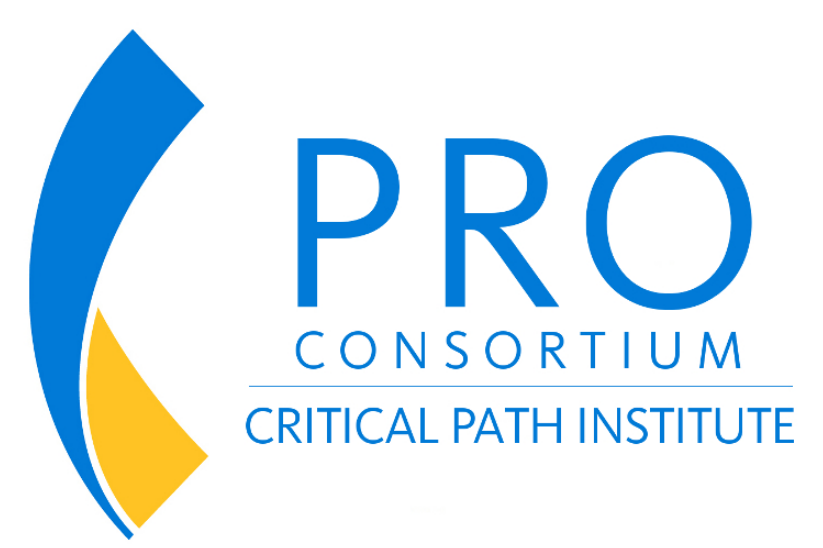


# Asthma Working Group



Presented at the Eighth Annual PRO Consortium Workshop – Bethesda, MD – April 26-27, 2017

## Background

### Rationale for Asthma Working Group (WG)

- Asthma was identified as an area for development of a novel PRO measure to support clinical trials. There is no standard PRO instrument that is qualified by the FDA for the purpose of measuring important symptoms of asthma.
- The Asthma WG is working to address this unmet need within FDA's COA Qualification Program by developing a PRO instrument for use in clinical trials of asthma therapies in accordance with the FDA PRO Guidance.

### Goal of the Asthma WG

- To develop a patient-reported diary to document daily asthma symptoms in adults and adolescents with a clinical diagnosis of mild to severe persistent asthma for use in clinical trials of asthma therapies as a co-primary or secondary endpoint measure to establish treatment benefit

### Targeted Labeling Language

<b>Overall</b>	<ul style="list-style-type: none"> <li>Patients treated with [drug X] reported significant reduction in asthma symptom severity</li> </ul>
<b>Daytime Symptoms</b>	<ul style="list-style-type: none"> <li>Patients treated with [drug X] reported significant reduction in daytime asthma symptom severity</li> <li>Patients treated with [drug X] reported significantly fewer days with asthma symptoms</li> </ul>
<b>Night-time Symptoms</b>	<ul style="list-style-type: none"> <li>Patients treated with [drug X] reported significant reduction in night-time asthma symptom severity</li> <li>Patients treated with [drug X] reported significantly fewer nights of awakenings due to asthma symptoms</li> </ul>

## Milestones

Milestone	Completed Date
Vendor selection and contracting	FEB 2012
Complete background research (Literature Review Report and Expert Panel Meeting)	SEP 2012
Draft Instrument: Complete initial qualitative research and generate items (concept elicitation interviews, item generation, expert panel input, and initial round of cognitive interviews)	AUG 2013
Submit Qualitative Research Summary Briefing Document to FDA for review and feedback	NOV 2013
Complete quantitative pilot study	OCT 2015
Complete data analysis and Quantitative Pilot Study Report	OCT 2016
Submit Qualification Briefing Package to FDA for exploratory use of ADSD	4Q 2016

## Highlights

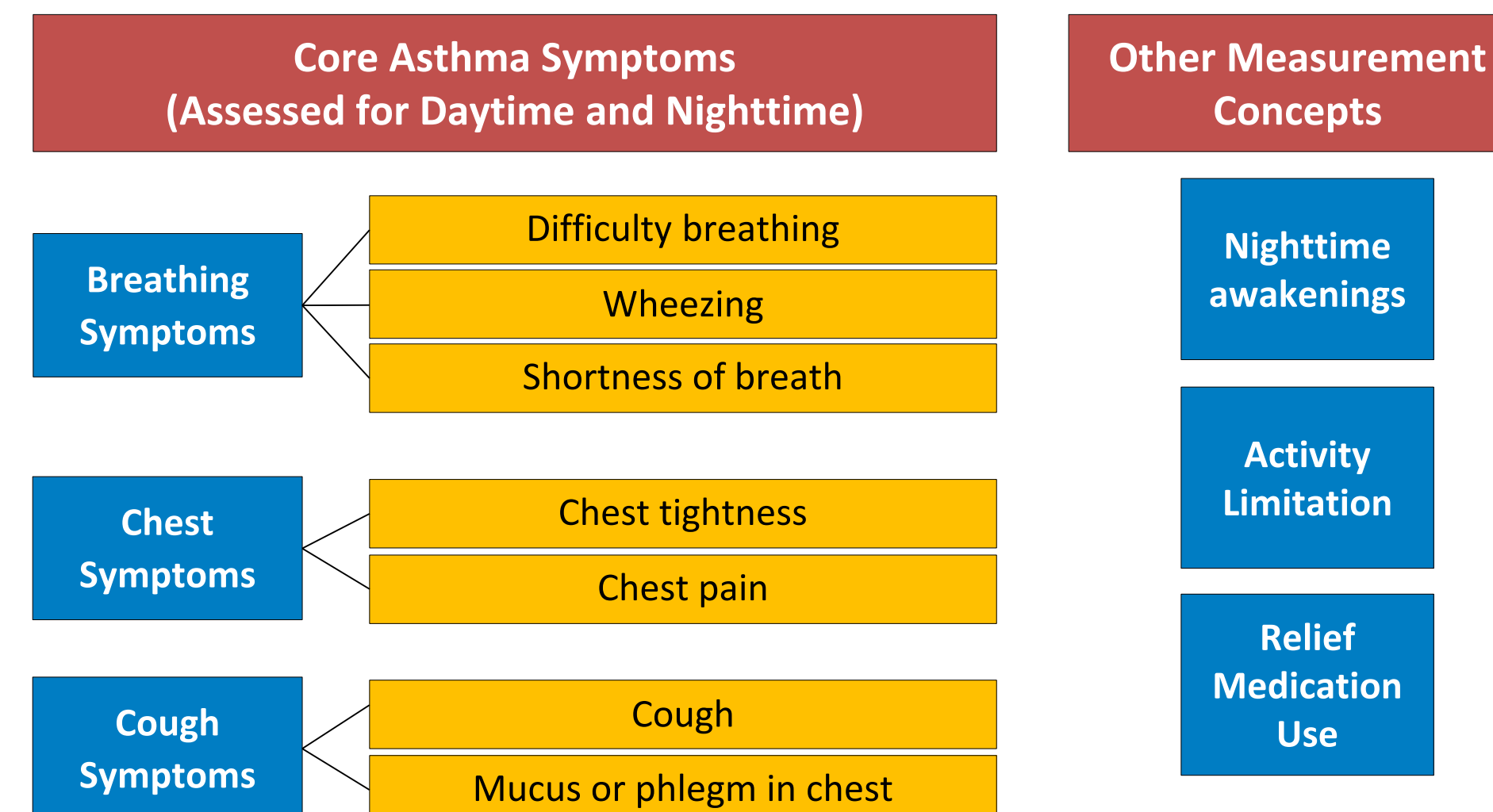
### Example Endpoint Model for Treatment of Asthma

Endpoint Hierarchy	Endpoint Concept(s)	Endpoint Type
Primary	Improvements in airflow obstruction <ul style="list-style-type: none"> <li>FEV<sub>1</sub></li> </ul> Reduction in asthma symptoms <ul style="list-style-type: none"> <li>Asthma total symptom score from <i>Asthma Daily Symptom Diary (ADSD)</i></li> </ul>	COA (PerFO) PRO - ADSD
Secondary	Daytime Symptoms <ul style="list-style-type: none"> <li>Proportion of days without symptoms based on <i>Asthma Daily Symptom Diary</i> (symptom free days)</li> </ul> Night-time Symptoms <ul style="list-style-type: none"> <li>Proportion of nights without asthma symptoms based on <i>Asthma Daily Symptom Diary</i></li> </ul>	PRO PRO

### Target Population

- Adolescents and adults aged 12 years and older with a clinical diagnosis of asthma with lung function impairment
- Patients across guideline-defined levels of disease severity, which include mild through severe persistent asthma (GINA, 2009)

### Conceptual Framework



### Measure – Asthma Daily Symptom Diary (ADSD)

**Core Items:** Seven items assessing three symptom domains  
 Note: Four supplementary items were developed related to asthma (night-time awakenings, activity limitations, relief inhaler use, nebulizer use) for optional use in clinical trials.  
**Recall Period:** Twice daily (morning and evening)  
**Response Options:** 11-point numeric rating scale  
**Symptom Attribute:** Severity was chosen (as opposed to frequency, duration, or bothersomeness) based on patient descriptions of asthma symptom experience.

## Working Group Updates

### Completed Activities

- Instrument review meeting held in January 2016, attended by expert panel and via teleconference by FDA. Objectives: review evidence and data collected from quantitative pilot study and exit interviews, and discuss initial analysis of item performance and instrument structure for the ADSD. Quantitative evidence was then considered with earlier qualitative findings and expert clinical input to make decisions regarding potential item reduction and scoring.
- Quantitative Pilot Study Report and quantitative data submitted to FDA in October 2016
- Qualification Briefing Package submitted to FDA in December 2016

### Information Dissemination

- Gater A, et al. Assessing Asthma Symptoms in Adolescents and Adults: Qualitative Research Supporting Development of the Asthma Daily Symptom Diary. *Value in Health* 2016;19(4):440-450
- Two posters will be presented at the American Thoracic Society International Conference 2017 on May 22, 2017 in Washington, DC:
  - Preliminary psychometric evaluation of the *Asthma Daily Symptom Diary (ADSD)*
  - Respondent understanding and user experience with the *Asthma Daily Symptom Diary (ADSD)*, a novel patient-reported outcome measure
- A manuscript reporting the results of the quantitative pilot study will be prepared for submission to *Chest* following qualification of the ADSD for exploratory use

### Next Steps

- Several WG sponsor clinical trials using the ADSD as an exploratory endpoint are underway
- Two WG teleconferences with FDA's Qualification Review Team to discuss FDA feedback on:
  - ADSD Quantitative Pilot Study Report
  - ADSD Qualification Briefing Package

## Working Group Participants

Company/Organization	Representatives
AstraZeneca AB	Niklas Karlsson, PhD; Sean O'Quinn
Boehringer Ingelheim	Mike Baldwin, MBA
Allergan	Robyn T. Carson, MPH
Genentech, Inc.	Alison Greene, MPH; Alison Matsui, MPH
GlaxoSmithKline, LLC	Linda Nelsen, MHS (Co-Chair); Margaret Tabberer, MSc; Richard Stanford, PharmD, MS
Janssen Global Services, LLC	Chenglong Han, MD, PhD
Merck Sharp & Dohme Corp.	Josephine Norquist, MS
Novartis Pharma AG	Luisa Álvares, MPharm; Thomas Martin, MD; Jessica Marvel, MPH
Pfizer, Inc.	Sheryl Pease, MBA, PMP
Sanofi	Adeline Abbe, MS; Asif Khan; Lauren Eckert
Expert Panel Members	Affiliation
Michael Schatz, MD	Kaiser Permanente, UCSD
Jerry Krishnan, MD, PhD	University of Chicago, NHLBI
John Haughney, MB	University of Aberdeen
Stuart Stoloff, MD	Fellow FAAAAI, Family Practitioner
Contract Research Organization	Research Team
Adelphi Values	Adam Gater, MSc; Rob Arbuckle, MSc; Nicola Bonner, MSc; Rebecca Hall, MMedSci; Gemma Barrett
ePRO System Provider	Representative
CRF Health	Paul O'Donohoe, BSc