DDT #000092 **REQUEST FOR INITIAL BRIEFING PACKAGE**

July 11, 2017

Carole A Tucker PhD
Temple University - College of Public Health
3307 North Broad Street
Philadelphia PA 19140
Email: tuckerc@temple.edu
Phone: 215.707.4877
FAX: 215.707.7500

Christopher B Forrest MD, PhD
The Children's Hospital of Philadelphia
3535 Market Street
Philadelphia PA
Email: forrestc@email.chop.edu
Phone: 267.426.6917

Regarding: DDT #000092 Letter of Intent for the PROMIS® Pediatric Crohn's Disease Short Form – Fatigue 10 – English version for use as a primary or secondary endpoint in phase 3 confirmatory superiority trials evaluating pediatric patients age 8-17 years with Crohn's Disease

Dear Drs. Tucker and Forrest:

We have completed our review of the Letter of Intent (LOI) submission for DDT COA #000092 dated January 29, 2017 and received on January 31, 2017 by the Clinical Outcomes Assessment Qualification Program. You have proposed the use of a tool to assess fatigue in pediatric patients age 8-17 years with Crohn's Disease using a patient-reported outcome.

We agree to enter this project into the CDER COA DDT qualification program. Please prepare an initial briefing package (IBP) that outlines your next steps. The attached Appendix 1 describes the summary information that we suggest be the focus of the initial briefing package. Following your next submission, we suggest having a teleconference to discuss the submission and provide additional consultation and advice.

The following responses address your specific questions:

1. Given the previous PROMIS outcome development and norming of this measure in the general pediatric population that included children with special health care needs in the proportion found in the general US population, does the Agency think that additional qualitative research is needed to support the content

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20903
www.fda.gov

validity of the PROMIS® pediatric fatigue scale in patients with Crohn's disease? If so, what and how much additional qualitative research evidence is needed to support content validity of the items?

We acknowledge the development history of PROMIS® including the qualitative research work already completed. An instrument is qualified for a specific context of use, which describes a complete and precise patient population and all other important criteria under which the DDT is adequate for use. The context of use is determined from review of both the qualitative and quantitative development work of the instrument. In order to determine if additional qualitative research is needed, you should describe in your initial briefing package the patient population used to develop the PROMIS® pediatric fatigue scale in Crohn's disease. Once reviewed, we will be able to determine if additional qualitative work is needed.

2. PROMIS® instruments are derived from IRT calibrated item banks developed using a rigorous mixed methods approach. PROMIS measures include short-forms (sub sets of items from the item bank) and computerized adaptive test (CAT) instruments (also a subset of items from the item bank). All instruments derived from the item bank provide scores on the same metric, allowing for score comparison across different instruments. What is the Agency's process for the qualification of the full item bank, specific short-form static instruments (as proposed here) versus CAT instruments?

At this time we believe that the short form and CAT versions of PROMIS® pediatric fatigue scale in Crohn's disease would consist of separate reviews. The short form may take less time to review than CAT. However, we are open to the exploration of a CAT based instrument for qualification. At this time, we are currently unsure of qualifying a full item bank until we have a better understanding of PROMIS® in disease specific populations. No matter what version of PROMIS ® (short-form or CAT) is selected, the instrument will need to be sensitive to detect a treatment effect.

3. Can the agency provide guidance on the balance of evidence in the dossier from the PROMIS instrument development as a universal (not disease specific) suite of measures relative to the evidence we are accumulating for Crohn's Disease as well as other pediatric health conditions in a variety of efforts? Is there potential to provide evidence across a variety of health conditions that would support the use of these measures as clinical outcomes in children with chronic illness?

We acknowledge the development history of PROMIS®; however, we will still need evidence from specific disease populations. We reference our response to question 1 as well.

If you have any questions, please contact the COA Staff via email at COADDTQualification@fda.hhs.gov. Please refer to DDT #000092.

Sincerely,

Michelle Campbell -S

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Date: 2017.07.11 14:16:57 -04'00'

Michelle Campbell, PhD, for
Elektra Papadopoulos, MD, MPH
Associate Director
Clinical Outcome Assessments Staff
Office of New Drugs
Center for Drug Evaluation and Research

Donna J. Griebel -S

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Donna Griebel, MD
Director
Division of Gastroenterology and Inborn Errors Products
Office of New Drugs
Center for Drug Evaluation and Research

Appendix 1: Initial Briefing Package Description

CLINICAL OUTCOME ASSESSMENT (COA) QUALIFICATION INITIAL BRIEFING PACKAGE

The COA qualification initial briefing package (IBP) should be accompanied by a cover letter (refer to section VII) and should include the following sections:

Section 1: Proposed Plan for COA Qualification

The following areas should be addressed for CDER review. The extent of information provided in each section will vary depending upon the evidence currently available to address each issue. We recommend for your initial briefing package you focus on the materials in section 1.1 to 1.6 below in order to facilitate discussion with the agency to ensure agreement before engaging in additional research. The additional information described below can be submitted in future submissions.

1.1 Introduction and overview

This should include a concise description of the disease and the clinical trial setting in which the COA would be used, the limitations of existing assessments, a brief description of the existing or planned COA, and the rationale for us e in drug development.

1.2 Concept of Interest for meaningful treatment benefit

Describe the meaningful aspect of patient experience that will represent the intended benefit of treatment (e.g., the specific symptom and/or sign presence or severity or limitations in performance or daily activities relevant in the targeted context of use)

Identify targeted labeling or promotional claims based on the COA (i.e., proposed claim wording)

Provide a conceptual framework for the outcome assessment(s)

1.3 Context of Use

Identify the targeted study population, including a definition of the disease and selection criteria for clinical trials (e.g., baseline symptom severity, patient demographics, language/culture groups)

Identify the targeted study design. Most commonly the COA will be used to assess the change (compared to a control) induced by a medical treatment.

Identify the targeted study objectives and endpoint positioning (i.e., planned set of primary and secondary endpoints with hierarchy). Usually, the COA will serve as a primary or secondary study endpoint.

1.4 Critical details of the measure to the degree known

Reporter, if applicable

Item content or description of the measure

Mode of administration

Data collection method

1.5 Overview of current COA development status (for existing measures or for measures already under development)

1.6 Description of the involvement of external expertise, including scientific communities or other international regulatory agencies, if applicable

Section 2: Summaries of Planned Studies or Completed Studies

2.1 Evidence of content validity (i.e., documentation that the COA measures the concept of interest in the context of use)

Development of the measure

- Literature input
- Expert input
- Reporter input (e.g., for PRO measures, concept elicitation, focus groups, or in-depth qualitative interviews to generate items, select response options, recall period, and finalize item content)
- Other input
- Justification for scoring algorithm (e.g., for multi-item COAs, the rationale and algorithm for how the items and domains are combined into a single score)
- For COAs with multiple versions, process for establishing that content validity is comparable between versions (e.g., COAs with multiple administration modes or methods)

2.2 Cross-sectional evaluation of measurement properties

Score reliability (including test-retest or inter-rater reliability)

Construct validity (comparison with other measures, e.g., patient and clinician global assessments)

2.3 Longitudinal evaluation of measurement properties

Longitudinal construct validity

Ability to detect change

2.4 Longitudinal evaluation to provide guidelines for interpretation of trial results

Evaluation of individual patient change (e.g., responder definition(s))

2.5 Language translation and cultural adaptation, if applicable

Process for simultaneous development of versions in multiple languages or cultures

Process for translation/adaptation of original version

Evidence that content validity is similar for versions in multiple languages

2.6 User manual, as available

Summary of current experience and known measurement properties in the targeted context of use

Administration procedures

Training materials

Scoring and interpretation procedures

Copy of all versions of the COA (or screen shots, if applicable)

2.7 Appendices (may include)

List of references and copies of only the most important references that the submitter feels CDER reviewers may want to review

Study documents (e.g., protocols, analysis plan, interview guide, data collection form(s))

Note: The link to appendices should be embedded in the relevant summaries.

Section 3: Questions

Specific questions for CDER