Clinical Outcome Assessments (COA) Qualification Program
DDT COA #000095: PROMIS® Pediatric Chronic Kidney Disease Short Form- Fatigue
Letter of Intent

Administrative Structure:

Description of the submitter including, but not limited to, principal investigator(s), working group member(s), institutions, and contact information not contained within the cover letter.

PEPR – FDA Workgroup Lead:
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The PEPR consortium workgroup members currently involved in the FDA approval process are: Carole A Tucker PhD, PEPR – FDA Workgroup Lead, Temple University - College of Public Health & Christopher B Forrest MD, PhD, PEPR Principal Investigator, Children's Hospital of Philadelphia.

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Concept(s) of Interest (COI) for Meaningful Treatment Benefit:

A description of the meaningful aspect of patient experience that will represent the intended benefit of treatment (e.g., presence/severity of symptoms, limitations in performance of daily activities).

The PROMIS® Pediatric Chronic Kidney Disease Short Form - Fatigue evaluates a range of self-reported symptoms, from mild feelings of tiredness to an overwhelming, debilitating and sustained sense of exhaustion that decreases one's ability to execute daily activities and function normally in family and social roles. The concept of fatigue is defined as experiences of feeling tired and the impact of those experiences on everyday life. The measure includes concepts of experiences of fatigue (frequency, duration and intensity), and the impact of fatigue on physical, mental, and social activities. The 8 items were selected from the existing PROMIS pediatric fatigue item bank, a universal measure. The PROMIS® Pediatric Fatigue item bank used as a basis for the Chronic Kidney disease short form underwent calibration on the general US population as part of the PROMIS effort. (https://www.niams.nih.gov/funding/Funded_Research/PEPR/).

Provide a conceptual framework for the COA(s)

To build the conceptual framework for the proposed COA, we identified conceptually distinct categories, or facets, based on the fatigue items that underwent psychometric testing during the development of the PROMIS pediatric fatigue item bank. Facets for pediatric fatigue include feelings of tiredness, feelings of weakness, sleeping, sports/exercise, climbing stairs, eating, bathing/showering, energy, fun, attention, memory, schoolwork, friendships, family, general activities, and performing tasks. Each facet may be evaluated by one or more items in the item bank. The results of semi-structured interviews with children with CKD support the relevance of this conceptual framework for the target population. Items in the short form were selected to cover a variety of facets of fatigue relevant to the target population.

Context of Use for COA Qualification:

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

In 2002, the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI) published a guideline on CKD, the NKF-K/DOQI Classification of the Stages of CKD. This classification provides stages of CKD severity, independent of cause, and applicable to children. The Work Group defined CKD as the presence of kidney damage or estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 for 3 months or more, irrespective of diagnosis. Kidney damage is usually identified by the presence of markers of disease that are present in blood, urine, or imaging studies, rather than by kidney biopsy. The CKD guidelines emphasize persistent proteinuria as a particularly important marker of kidney damage. Our PEPR validation study includes children in stages 2 – 4 with two eGFR readings in the range of 15-89 mL/min/1.73 m^2 at least 3 months apart.

Patient demographics – Children between 8 – 17 years of age, with no restrictions on gender, race and ethnicity

Language/culture group – General US population, English speaking

Baseline symptom severity – All levels of severity and disease activity

Comorbidities – No restrictions

***Targeted study design and statistical analysis plan (includes the role of the planned COA in future drug development clinical trials, including the planned set of primary and secondary endpoints with hierarchy, if appropriate*).**

The **PROMIS® Pediatric Chronic Kidney Disease Short Form - Fatigue** can be used in future drug development trials as a primary, co-primary, or secondary endpoint in studies that use pharmacological interventions to improve the fatigue associated with CKD.

Applicable study settings for future clinical trials

- ***Geographic location with language/culture groups***
    - United States & Canada, all genders, races and ethnicities, English speaking
    - The **PROMIS® Pediatric Chronic Kidney Disease Short Form - Fatigue** is a fixed-length short form for child-report developed using mixed methods that consists of 8 Likert response items that can be administered using electronic data capture methods or by paper/pencil. We propose its intended initial use to be in outpatient settings in the United States and Canada across all racial and ethnic groups. The submitted **PROMIS® Pediatric Chronic Kidney Disease Short Form** is intended for English speaking respondents. As noted in the translation section below, the measure has been culturally harmonized and translated into Dutch, English, French, German, Italian, Simplified Chinese (Mandarin), and Spanish.

- ***Other study setting specifics (e.g., inpatient versus outpatient)***
  Outpatient setting only in our initial efforts.

<u>COA Type:</u> PRO