Clinical Outcome Assessments (COA) Qualification Program
DDT COA #000112: Chronic Heart Failure- Symptom Scale (CHF-SS)
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.

This proposal is being submitted by the Patient-Reported Outcome (PRO) Consortium at the Critical Path Institute (C-Path).

The PRO Consortium enables pre-competitive collaboration that leverages human and financial resources from multiple stakeholders. The PRO Consortium's Chronic Heart Failure (CHF) Working Group currently has members representing the following pharmaceutical firms: Amgen, AstraZeneca, Bayer, Ironwood, Janssen, Lilly, Merck, and Sanofi. The initial development work for the measures being proposed for entry into the qualification program was funded by Amgen and conducted by Evidera. C-Path's principal investigator is Stephen Joel Coons, PhD, Executive Director of the PRO Consortium.

Contact Information:
Stephen Joel Coons, Ph.D.
Executive Director, PRO Consortium
Critical Path Institute
1730 E. River Road
Tucson, Arizona 85718-5893
520-547-3455 Fax: 520-547-3456
sjcoons@c-path.org

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

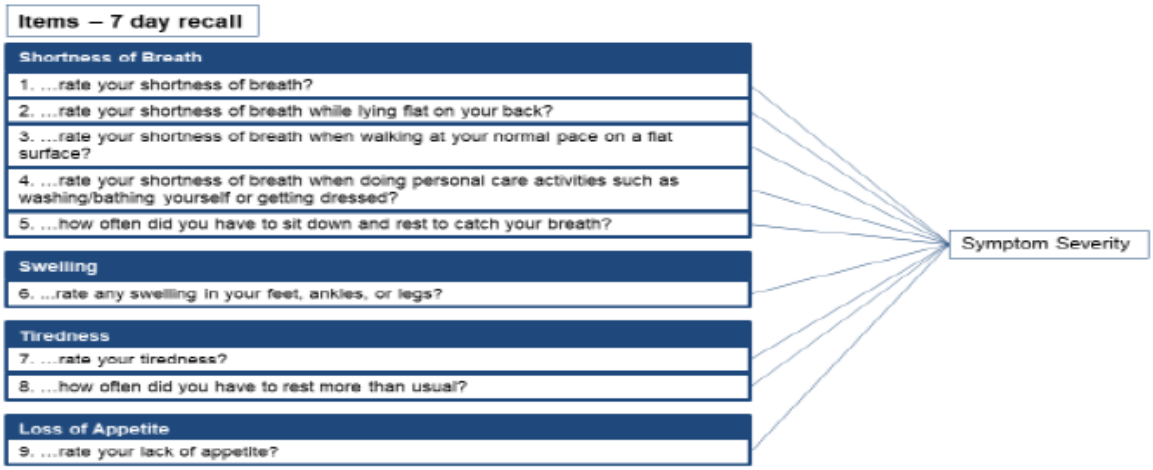
A description of the meaningful aspect of patient experience that will represent the intended benefit of treatment (e.g., presence/severity of symptoms, limitations in performance of daily activities).

The concepts of interest for the PRO measures are the self-reported severity of chronic heart failure symptoms and the self-reported impact of chronic heart failure symptoms on physical functioning. The concept of interest for the activity monitor-based endpoint measure is physical activity with specific variables to be determined.

Provide a conceptual framework for the COA(s).

Figure 1 provides the hypothesized conceptual framework for the 9 items of the *Chronic Heart Failure- Symptom Scale* (*CHF-SS*).

Figure 1. Hypothesized Conceptual Framework for the *CHF-SS*



COU 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)

The *CHF-SS*, *CHF-IS*, and activity monitor-based endpoint measure are intended to assess changes in CHF symptom severity, symptom impact on physical function, and physical activity for adults who have been diagnosed with CHF.

The target population includes adults with a clinician-confirmed history of chronic heart failure for ≥3 months with New York Heart Association class II–IV symptoms for ≥4 weeks as confirmed by medical records, confirmed and documented diagnosis of chronic heart failure with preserved ejection fraction (HFpEF) or chronic heart failure with reduced ejection fraction (HFrEF), in stable condition for at least 4 weeks, and treated with stable, optimal pharmacological therapy for a minimum of 4 weeks prior to screening.

***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 scores resulting from the proposed PRO measures and activity monitor-based endpoint measure will be positioned to derive key endpoints in CHF treatment trials. Future research will explore whether the PRO measure and activity monitor-based endpoint measure scores will be combined to create a composite score or composite endpoint or scored separately to support separate endpoints.

The specific endpoint selection, positioning, and measurement approach will be determined by the study sponsor in concert with the appropriate regulatory review agencies.

A statistical analysis plan for a CHF treatment trial cannot be developed in the absence of a specific study protocol, which does not exist at this time.

Applicable study settings for future clinical trials

- ***Geographic location with language/culture groups***

The *CHF-SS* and *CHF-IS* will be translated for use outside the U.S. and are intended for use in multinational trials or trials within a single country where multiple language and cultural groups may be enrolled. The activity monitor-based endpoint measure is also intended to be used in multinational trials or within a single country with multiple language or cultural groups.

- ***Other study setting specifics (e.g., inpatient versus outpatient)***

The target population is adult CHF patients with stable reduced or preserved ejection fraction (NYHA class II-IV) who are being treated on an outpatient basis.

<u>COA Type:</u> Patient-Reported Outcome (PRO)