Clinical Outcome Assessments (COA) Qualification Program
DDT COA #000109: Symptoms of Major Depressive Disorder Momentary Assessment (SMDDMA)
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. At this time, the PRO Consortium's Depression Working Group has members representing the following pharmaceutical firms: Allergan, Boehringer Ingelheim Pharmaceuticals, Inc., and Janssen Pharmaceutical Companies of Johnson & Johnson. C-Path's principal investigator is Stephen Joel Coons, PhD, Executive Director of the PRO Consortium.

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

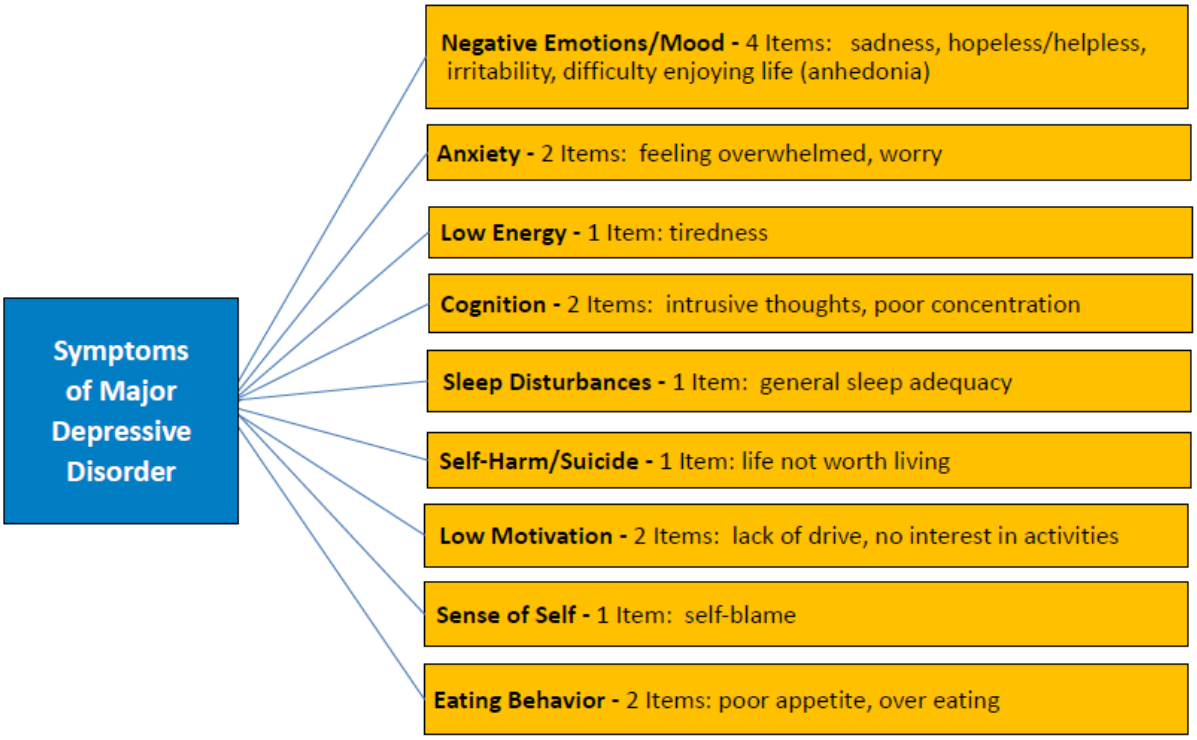
A description of the meaningful aspect of patient experience that will represent the intended benefit of treatment (e.g., presence/severity of symptoms, limitations in performance of daily activities).

With FDA qualification of the *Symptoms of Major Depressive Disorder Scale (SMDDS) v1.0* in November 2017, the Depression Working Group is now pursuing qualification of a new measure derived from the *SMDDS v1.0* that will have a 24-hour recall period rather than a 7-day recall period. Hence, the concept of interest is self-reported depression symptom severity in adults during the past 24 hours. The provisional name of the new measure derived from the *SMDDS v1.0* is the *Symptoms of Major Depressive Disorder Diary* (*SMDDD*). The proposed conceptual framework below contains the core symptoms of major depressive disorder (MDD) that were identified in the literature, supported by clinical experts, and found to be most relevant to patients who have been diagnosed with and treated for this condition.

Provide a conceptual framework for the COA(s).

The figure below provides an overview of the relationship of the 16 items and 9 domains of the *SMDDD*.

Conceptual Framework for the Proposed 16-Item *Symptoms of Major Depressive Disorder Diary (SMDDD)*



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 *SMDDD* is intended to assess changes in depressive symptom severity for adults who have been diagnosed with MDD. The target population includes adults (aged 18 to 65 years of age) with a clinical diagnosis of MDD, who are being treated in an ambulatory setting. Other characteristics of this target population include those who have experienced a major depressive episode within the previous 6 months, have a Hamilton Depression Rating Scale (HAM-D) score >18 or Montgomery-Åsberg Depression Rating Scale (MADRS) score >19, and meet the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for MDD.

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)

It is expected that the resulting endpoint (change in symptom severity), as measured by the SMDDD, may be used as a primary or co-primary endpoint to establish treatment benefit, or as a secondary endpoint to support labeling claims from data produced in randomized controlled clinical trials where an experimental treatment for MDD is being tested. Comparisons can be made to both placebo groups and comparator drug groups depending on the number of arms in the clinical trial.

The intent is to use the SMDDD to assess treatment benefit in clinical trials for MDD therapies that may have a faster onset of action and potentially communicate this earlier antidepressant treatment benefit in the product label. Other clinical measures, such as a clinician-reported outcome (ClinRO) assessment, may serve as the source of primary or co-primary endpoints alongside the SMDDD as a measure of symptom severity. In instances where the SMDDD is employed to derive a secondary endpoint, the clinical trial would need to succeed on the clinician-reported endpoint before success could be attained on the secondary endpoint relating to patient-reported symptom severity.

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

A statistical analysis plan for a MDD 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 SMDDD will be translated for use outside the U.S. and is intended for use in multinational trials or trials within a single country where multiple language and culture groups may be enrolled

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

The target population is adults from 18 to 65 years of age who have been diagnosed and are being treated in an ambulatory setting for MDD.

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