Depression Working Group 2.0

12th Annual PRO Consortium Workshop – Held Virtually on April 14-15, 2021

PRO CONSORTIUM
CRITICAL PATH INSTITUTE

Background

Rationale for Depression Working Group 2.0

- Due to the emergence of antidepressant agents with faster onsets of action, there is growing recognition of the need for well-defined and reliable assessment tools that can measure clinical benefit within shorter timeframes, potentially within hours or days rather than weeks in treatment trials for major depressive disorder (MDD).
- With FDA qualification of the 7-day recall period *Symptoms of Major Depressive Disorder Scale (SMDDS)* in November 2017, the Depression Working Group 2.0 is developing 24-hour recall and momentary assessment (i.e., assessment of the severity of an MDD symptom "at this moment") measures based on the *SMDDS*.

Goal of the Depression Working Group 2.0

- The Depression Working Group 2.0's main focus is to pursue qualification of the new 24-hour recall measure, which is provisionally named the *Symptoms of Major Depressive Disorder Diary* (*SMDDD*).
- A secondary focus is to pursue qualification of a new momentary assessment measure, which is provisionally named the *Symptoms of Major Depressive Disorder Momentary Assessment* (*SMDDMA*).

Concept of Interest

- *SMDDD*: self-reported depression symptom severity in adults during the past 24 hours.
- *SMDDMA:* self-reported depression symptom severity in adults at the time the self-assessment is completed (i.e., "at this moment").

Targeted Labeling Language

- Patients treated with [*Drug X*] reported clinically significant reductions in severity of major depressive disorder compared with treatment [*YY*]. (*Based on group comparisons of means*)
- Compared with [*YY*], significantly more patients treated with [*Drug X*] reported clinically meaningful reductions in severity of major depressive disorder. (*Based on group comparison using responder analysis*)
- Compared with [*YY*], patients treated with [*Drug X*] reported significantly fewer days with symptoms of major depressive disorder. (*Based on group comparison of number of days to clinically meaningful response*)
- Compared with [YY], patients treated with [Drug X] reported significantly faster relief of symptoms of major depressive disorder. (*Based on group comparison of time to clinically meaningful response*)

Milestones

Milestone	Target Date	Completed Date
Letter of Intent submission for *SMDDD* and *SMDDMA* to FDA		OCT 2018
Acceptance of *SMDDD* and *SMDDMA* by FDA into the COA Qualification Program		FEB 2019
FDA meeting to discuss preliminary feedback on cognitive interview report		MAY 2020
Qualification Plan submission for *SMDDD* to FDA	Q2 2021	
Qualification Plan submission for *SMDDMA* to FDA	Q3 2021	
Full Qualification Package submission for *SMDDD* to FDA	TBD	
Full Qualification Package submission for *SMDDMA* to FDA	TBD	

Highlights

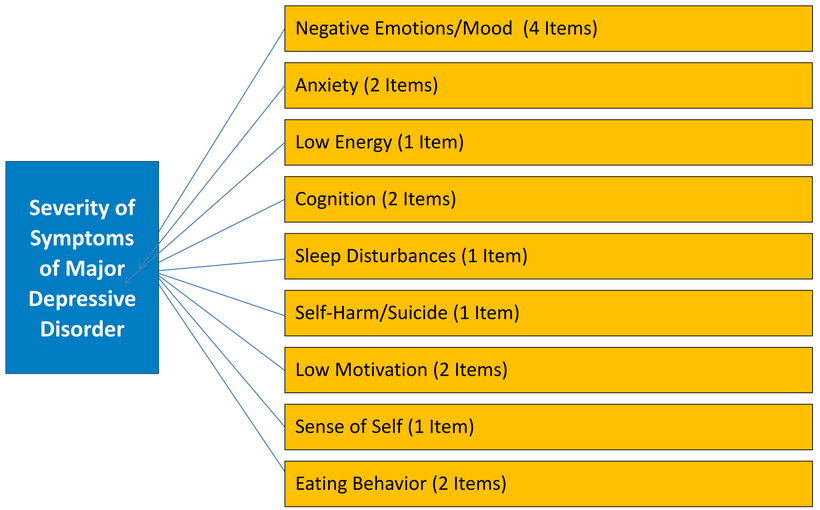
Example Endpoint Model for Treatment of Depression

Endpoint Hierarchy	Endpoint Concept(s)	Endpoint Type
Primary	Severity of symptoms of major depressive disorder	PRO (*SMDDD*, *SMDDMA*)
Secondary	Affect Disease activity	ClinRO ClinRO

Target Population

- Persons 18 years and older, being treated in ambulatory settings, with a diagnosis of major depressive disorder (depression) with or without significant disability that impairs productivity in school, workplace, or in other customary activities, that would be expected to reduce patients' quality of life and life satisfaction, and may engender suicidal ideation

Hypothesized Conceptual Framework for the *Symptoms of Major Depressive Disorder Diary* (*SMDDD*)



Measure – *Symptoms of Major Depressive Disorder Diary* (*SMDDD*)*

Number of Items: 16 addressing 9 symptom domains

Recall Period: Past 24 hours

Response Options: 5-level verbal rating scale

Symptom Attribute: Intensity or frequency as a measure of severity

Data Collection Mode: Electronic data collection, specific mode to be determined

*The current version of the *SMDDMA* includes 11 items addressing 7 symptom domains that are suitable for momentary assessment. All item concepts from the *SMDDD* are represented within the *SMDDMA* except for 1 negative emotions/mood item, 1 cognition item, 1 sleep disturbance item, and 2 eating behavior items.

Working Group Activities

Completed Activities

- The working group modified *SMDDS* items to work within the shorter recall of the new measures. In addition to modifications associated with recall period made to item wording:
  - revisions were made to 2 items to create the *SMDDD,* but all concepts were retained;
  - revisions were made to 4 items and 4 items were dropped to create the *SMDDMA*.
- Two Letters of Intent were submitted to FDA in October 2018.
- FDA accepted the *SMDDD* and *SMDDMA* into COA Qualification Program in February 2019.
- A cognitive interview study was subsequently conducted to obtain the additional qualitative evidence necessary to refine the original content for shorter recall periods.
  - Nineteen qualitative interviews were completed in 4 iterative waves.
  - Based on evidence that emerged from the interviews, the development team agreed to revise one *SMDDD* item and drop one *SMDDMA* item.
  - The resulting 16-item *SMDDD* and 11-item *SMDDMA* were found to contain the relevant and suitable core symptom content for the specific recall period context.
- The cognitive interview report was submitted to FDA in March 2020 for feedback about whether qualitative results, together with supporting evidence from the qualified *SMDDS*, were adequate to move forward with development of the Qualification Plans.
- In May 2020, the working group met with FDA to discuss FDA's feedback.
  - As a result of this discussion, one item of the *SMDDMA* was modified to align with *SMDDD* wording for consistency.
- FDA subsequently agreed that it was appropriate to proceed with development of Qualification Plans for both the *SMDDD* and *SMDDMA*.
- C-Path was awarded FDA Drug Development Tools Research Grant funding in July 2020 to develop the Qualification Plan for the *SMDDMA*.

Challenges

- Since the *SMDDMA* evaluates self-reported MDD symptom severity at the time the self-assessment is completed, a challenge within the cognitive interview phase was determining 1) which concepts participants believed were truly relevant in a momentary assessment context and 2) how the items should be worded accordingly in that context.
- One challenge has been to determine how best to collect quantitative data for the *SMDDMA* in a non-interventional setting to evaluate measurement properties (i.e., in a quantitative pilot study).
- Another challenge will be to determine the appropriate way to use the MDD symptom measures together in a clinical trial setting in terms of the appropriate baseline and follow up measures (as item concepts were, in fact, removed from the *SMDDMA* because they were not feasible in the shorter recall context so not all concepts are present).

Next Steps

- *SMDDD* and *SMDDMA* will be included in a combined quantitative pilot study in which their psychometric properties will be evaluated.
- Submit draft quantitative study protocol synopsis to FDA for feedback
- Prepare and submit Qualification Plans for *SMDDD* and *SMDDMA* to FDA

Working Group Participants

Company/Organization	Representative
AbbVie	Jonathan Stokes, MBA; Sara Higa, PharmD, MSc
Janssen Research & Development, LLC	Carol Jamieson, BSc; Heather Rozjabek, PhD, MPH
Boehringer-Ingelheim	Giancarlo Maranzano, PharmD
Affiliation	**Other Participants**
National Institute of Mental Health	Sarah Hollingsworth Lisanby, MD
Research Partner	**Research Team**
Evidera	Mona Martin, RN, MPA; Don Bushnell, MA