Depression Working Group 2.0

Prepared for the 11th Annual PRO Consortium Workshop (April 22-23, 2020), which was cancelled due to COVID-19

PRO CONSORTIUM
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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 with treatment trials for major depressive disorder (MDD).
- With FDA qualification of the *Symptoms of Major Depressive Disorder Scale (SMDDS)* in November 2017, the Depression Working Group 2.0 is exploring the use of the *SMDDS* items to derive new measures for a 24-hour recall period as well as for momentary assessment (i.e., assessment of the severity of an MDD symptom "at this moment").

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* is self-reported depression symptom severity in adults during the past 24 hours.
- *SMDDMA* is 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
Interim submission of cognitive interview study report to FDA to obtain preliminary feedback		MAR 2020
Qualification Plan submission for *SMDDD* to FDA	Q4 2020	
Qualification Plan submission for *SMDDMA* to FDA	TBD	
Full Qualification Package submission for *SMDDD* to FDA	TBD	
Full Qualification Package submission for *SMDDMA* to FDA	TBD	

Highlights

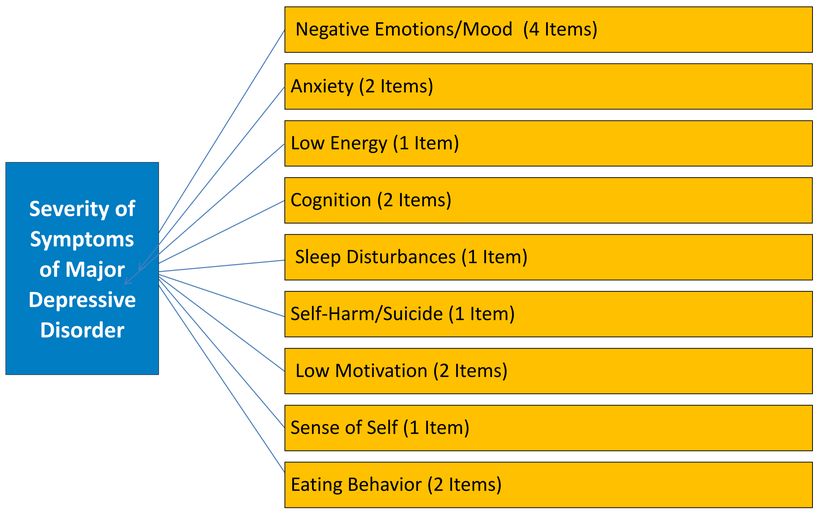
Example Endpoint Model for Treatment of Depression

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

- Patients 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 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 worked with Health Research Associates (HRA; now Evidera) to modify the *SMDDS* items to function properly within the shorter recall of the two new measures. In addition to obvious modifications associated with recall period that were made to the 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 agreed to accept the *SMDDD* and *SMDDMA* into the 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 four 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* have been shown to be properly understood by participants from the target population and to contain the relevant and suitable core symptom content for the specific recall period context.
- C-Path submitted a Drug Development Tools Research Grant application to FDA in April 2020 seeking funding 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.
- For the *SMDDMA*, a question remains whether it will be possible to collect quantitative data in a non-interventional setting to evaluate measurement properties (i.e., in a quantitative pilot study) because the target population would need to include extremely severe and potentially treatment resistant participants who would be difficult to recruit for this type of study outside of a treatment or clinical trial setting.
- 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 quantitative research in which their psychometric properties will be evaluated.
- Submit Qualification Plan for *SMDDD* to FDA in 2020
- Submit Qualification Plan for *SMDDMA* to FDA: Target 2021

Working Group Participants

Company/Organization	Representative
Allergan	Amy Tung, PharmD; Jonathan Stokes, MBA; Robyn Carson, MPH
Janssen Global Services LLC	Carol Jamieson, BSc
Boehringer-Ingelheim	Giancarlo Maranzano, PharmD; Matthew Sidovar, MSc, MA
Contract Research Organization	**Research Team**
Evidera	Mona Martin, RN, MPA; Don Bushnell, MA