Depression Working Group 2.0

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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 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

- The concept of interest of the *SMDDD* is self-reported depression symptom severity in adults during the past 24 hours.
- The concept of interest of the *SMDDMA* is self-reported depression symptom severity in adults at the time the self-assessment is completed.

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)*

Milestones

Milestone	Expected Date	Completed Date
Submit Letters of Intent (LOI) to FDA		OCT 2018
FDA accepts *SMDDD* and *SMDDMA* into the qualification program		FEB 2019
Complete cognitive interview study	Q3 2019	
Submit Qualification Plan for *SMDDD* to FDA	TBD	
Submit Qualification Plan for *SMDDMA* to FDA	TBD	
Submit Full Qualification Package for *SMDDD* to FDA	TBD	
Submit Full Qualification Package for *SMDDMA* to FDA	TBD	

Highlights

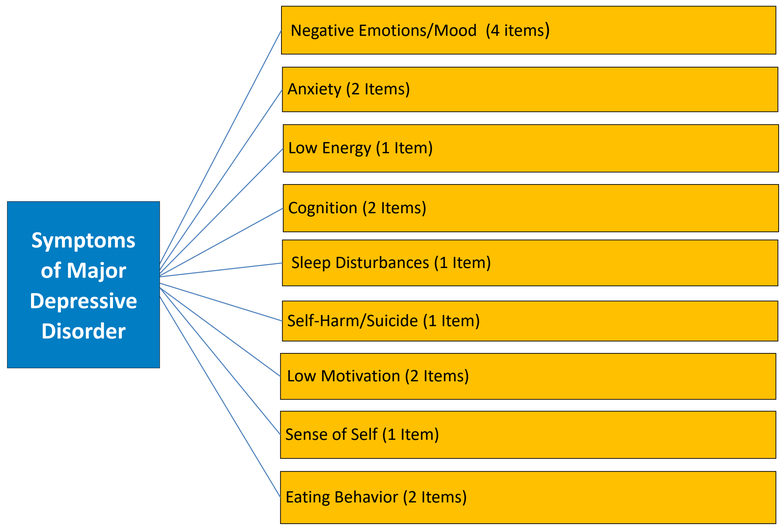
Example Endpoint Model for Treatment of Depression

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

Core Items: 16 items 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 12 items addressing 7 symptom domains that are suitable for momentary assessment. All concepts from the *SMDDMS* are represented within the *SMDDMA* except for 1 cognition item, 1 sleep disturbance item, and 2 eating behavior items.

Working Group Activities

Completed Activities

- The WG 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 the obvious modifications associated with recall period that were made to the text…
  - revisions were made to 2 items to create the *SMDDD,* and all concepts have been retained so far, and
  - revisions were made to 4 items and 4 items were dropped to create the *SMDDMA*.
- Two Letters of Intent were submitted to FDA in December 2018.
- FDA agreed to enter the *SMDDD* and *SMDDMA* into the COA Qualification Program in February 2019.
- A cognitive interview study is currently under way. The goal of these qualitative interviews is to further evaluate the content validity of the *SMDDD* and *SMDDMA* and ensure that respondents can understand/comprehend the revised items.
  - Fifteen of the planned qualitative interviews have been completed, with a final wave of five interviews to be conducted.

Unique Issues for the Working Group

- Clinical trial study designs for new fast-acting treatments for MDD seek to detect clinical benefit as quickly as possible, which requires the ability to measure symptoms at different timepoints after treatment is administered. The *SMDDD* and *SMDDMA* provide flexibility to assess symptoms daily or at several points within a day.
- As the *SMDDMA* evaluates self-reported MDD symptom severity at the time the self-assessment is completed, a challenge within the ongoing cognitive interview phase is aiming to determine which concepts are truly relevant in a momentary assessment setting from the patient participant perspective and how to word them accordingly.
- For the *SMDDMA*, it may not be possible to collect adequate data in a non-interventional setting to evaluate measurement properties (i.e., 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 symptoms measures together in a clinical trial setting in terms of the appropriate baseline and follow up measures (if item concepts are, in fact, removed from the *SMDDD* or *SMDDMA* because they are not feasible in the shorter recall context).

Next Steps

- Additional cognitive interviews with the *SMDDD* and *SMDDMA* are being conducted to obtain the additional qualitative evidence necessary to refine the original content for shorter recall periods.
- Submit Qualification Plan for *SMDDD* to FDA in 2019

Working Group Participants

Company/Organization	Representative
Allergan	Amy Tung, PharmD; Jonathan Stokes, MBA; Robyn Carson, MPH
Janssen Global Services	Carol Jamieson, BSc
Boehringer-Ingelheim	Giancarlo Maranzano, PharmD; Matthew Sidovar, MSc, MA
Contract Research Organization	**Research Team**
Health Research Associates, Inc. (now Evidera)	Mona Martin, RN, MPA; Don Bushnell, MA; Carla Ascoytia, BA