Depression Working Group 2.0

13th Annual PRO Consortium Workshop – Held Virtually on April 13-14, 2022

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 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 primary 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
Letters 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
Cognitive interview study report submission to FDA		MAR 2020
Qualification Plan submission for *SMDDD* to FDA	Q2 2022	
Qualification Plan submission for *SMDDMA* to FDA	Q3 2022	
Full Qualification Package submission for *SMDDD* to FDA	TBD	
Full Qualification Package submission for *SMDDMA* to FDA	TBD	

Highlights

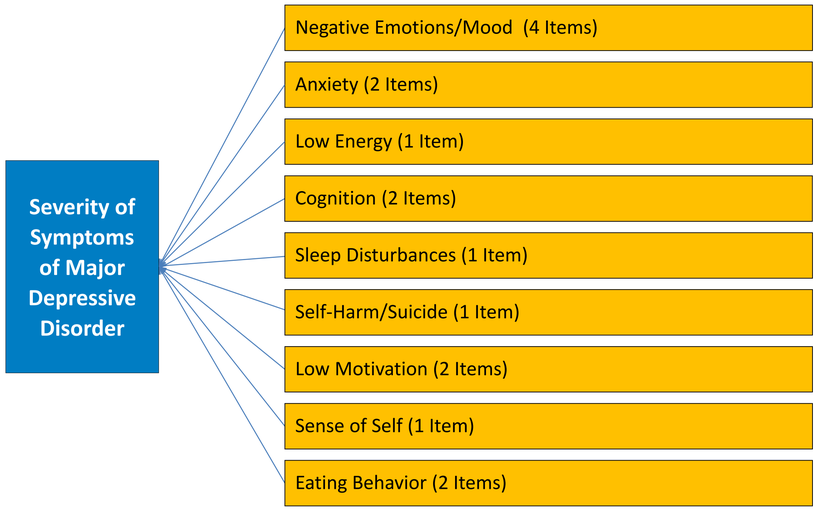
Example Endpoint Model for Treatment of Depression

Endpoint Hierarchy	Endpoint Concept(s)	Endpoint Type
Primary	Severity of symptoms of MDD	PRO (*SMDDD*)
Secondary	Time to early symptom improvement	PRO (*SMDDMA*)
	Affect	ClinRO
	Disease severity	ClinRO

Target Population

- Persons 18 years and older with a diagnosis of MDD (depression), who are being treated in ambulatory settings

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. Symptom attribute is intensity.

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*.
- 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.
- Received grant funding to develop *SMDDMA* Qualification Plan in July 2020.

Substantive FDA Interactions

- Following submission of the cognitive interview study report to FDA to confirm that qualitative results together with supporting evidence from the qualified *SMDDS* were adequate to move forward with development of the Qualification Plans, the working group met with FDA's Qualification Review Team (QRT) in May 2020 to discuss their feedback.
  - As a result of this discussion, one item of the *SMDDMA* was modified to align with *SMDDD* wording for consistency.
  - 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.
  - FDA subsequently agreed that it was appropriate to proceed with development of Qualification Plans for both the *SMDDD* and *SMDDMA*.
- A meeting was held with FDA's QRT in July 2021, following submission by the working group of a combined *SMDDD* and *SMDDMA* quantitative pilot study protocol synopsis, including evaluation of psychometric properties. After discussion of the proposed study design, FDA agreed it was appropriate to include both measures in one combined study.

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

- Prepare and submit Qualification Plans for *SMDDD* and *SMDDMA* to FDA
- Conduct combined quantitative pilot study including *SMDDD* and *SMDDMA*

Working Group Participants

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