# Depression Working Group 2.0

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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 time frames, 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 a key subset 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 | | JUL 2022 |
| Qualification Plan submission for *SMDDMA* to FDA | | MAR 2023 |
| Full Qualification Package submission for *SMDDD* to FDA | TBD | |
| Full Qualification Package submission for *SMDDMA* to FDA | TBD | |

## Highlights

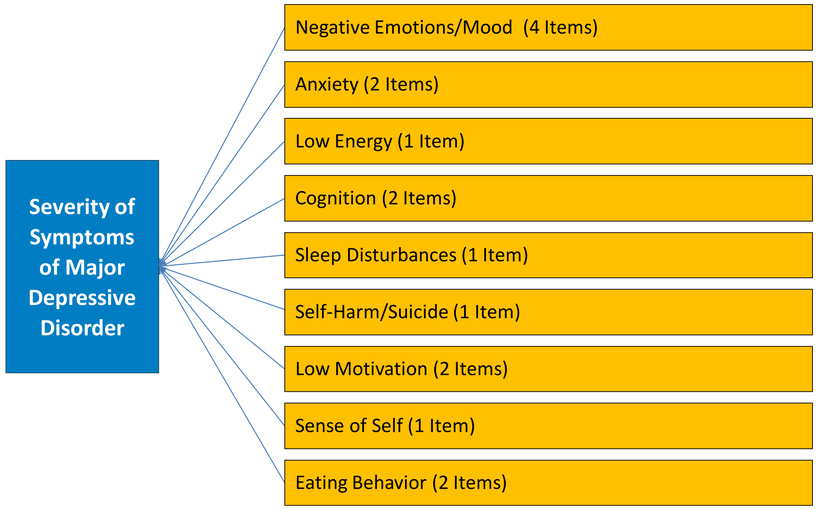
### Example Endpoint Model for Treatment of Depression

| Endpoint Hierarchy | Endpoint Concept(s) | Endpoint Type |
|---|---|---|
| Primary | Severity of MDD symptoms | PRO (*SMDDD*) |
| | MDD disease severity | ClinRO |
| Secondary | Time to improvement for key subset of MDD symptoms | PRO (*SMDDMA*) |
| | Affect | ClinRO |
| | MDD 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

### Measure – *Symptoms of Major Depressive Disorder Momentary Assessment* (*SMDDMA*)

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 for the shorter time frames of the new measures. In addition:
  - 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 time frames.
  - 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.
- Qualification Plans (QPs) were submitted to FDA for *SMDDD* (July 2022) and *SMDDMA* (March 2023).

### 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 QPs, 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 time frame.
  - FDA subsequently agreed that it was appropriate to proceed with development of QPs 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 context of a shorter time frame so not all concepts are present).

### Next Steps

- FDA will conduct reviewability assessment followed by review of each QP.
- 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; Maarten Voorhaar, MSc |
| **Affiliation** | **Other Participants** |
| National Institute of Mental Health | Sarah Hollingsworth Lisanby, MD |
| **Research Partner** | **Research Team** |
| Evidera | Mona Martin, RN, MPA; Don Bushnell, MA |