

## CASE STUDY:

# SIGNANT SMARTSIGNALS eCOA – CENTRAL REVIEW

Leveraging central clinician ratings to assess and improve the reliability of site-rating of major depressive disorder patients

### OVERVIEW:

Signant's Central Review service conducted independent expert evaluation of site-administered Montgomery-Asberg Depression Rating Scale (MADRS) assessments across five major depressive disorder (MDD) clinical trials. Based on audio recordings of site-based interviews, Signant's expert central raters provided their own independent ratings to compare against the original site scores. This quality control process enabled targeted remediation training to site raters, and ensured assessment consistency throughout the studies—ultimately improving endpoint data reliability.

### EVALUATION SUMMARY:

**Number of studies:** 5

**Study Phases:** Phase 2 and Phase 3

**Therapeutic area:** Major depressive disorder (MDD)

**Patient population:** Adults, aged 18 – 75

**Primary endpoint:** Montgomery-Asberg Depression Rating Scale (MADRS)

**Number of patients:** 500+

**Number of site raters:** 390+

**Countries:** USA, Canada, Russia, Serbia, Ukraine, UK, Australia

### INTRODUCTION

Primary endpoints in psychiatric trials are commonly comprised of the scores derived from clinician ratings using standardized rating instruments. To optimize the power of the clinical trial to detect treatment-related differences, it is important to consider approaches to limiting inter-rater and intra-rater variability. In addition to comprehensive rater training and qualification programs, the use of site-independent central raters to assess ongoing reliability of site ratings and mitigate concerns can improve the through-study accuracy and consistency of ratings and improve signal detection.

This evaluation served to demonstrate the value of central ratings for enhanced quality control in reference to five phase 2 and 3 studies in MDD using the MADRS to measure severity of depressive symptoms.

## METHODS

All raters (397 site raters, and 42 site-independent raters) involved in the studies underwent comprehensive rater training and qualification. For quality control, each study included a central review using independent ratings based on audio recordings of the site interviews. Independent ratings were performed in a randomized manner, and blinded to site, study visit, and site-rater score. Independent and site-based ratings were compared to evaluate the reliability and accuracy of site-based clinician ratings, providing enhanced levels of quality control for the study. Site-based raters who were frequently associated with divergent scores compared to the site-independent ratings were provided additional telephone-based training to remediate.

## RESULTS

Central reviews were performed on 3,736 MADRS assessments, and were highly correlated to the site-based assessments across all study visits. Of these, 249 (6.6%) of independent assessments showed a 6-point or greater deviation from the site rating. The reason for most rating discrepancies was usually a failure to apply scoring conventions, or interviews of insufficient length to conduct a comprehensive assessment. Subsequent review of site-based rater performance following telephone remediation revealed greater scoring concordance with the central rater in almost every case.

## CONCLUSIONS

This analysis confirms the value of audio recording of site-based interviews as a surveillance strategy for quality assurance using central site-independent raters to identify rating deviations and enable in-study remediation training where needed.

## PUBLICATION

Targum SD, Catania CJ. Audio-digital recordings for surveillance in clinical trials of major depressive disorder. *Contemp Clin Trials Commun.* 2019; 14: 100317.

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