



## case study:

### **i3 CLINICAL TRAINING AND ASSESSMENT GROUP IMPROVES DATA VALIDITY, YIELDS ONLY POSITIVE PIVOTAL STUDY**

#### **Challenge: Maintain precision in parallel panic disorder studies with 95 European sites.**

A sponsor was conducting two parallel panic disorder studies to assess the efficacy of an antidepressant across 95 sites throughout Europe. i3 CNS was selected as a full-service CRO for one pivotal study, while a separate CRO was chosen for the parallel study. Additionally, the i3 Clinical Training and Assessment (CTA) group was provided rater-training services for both of these studies.

The trials, which randomized 625 patients over a 12-month enrollment period, surpassed all contracted milestones. However, a routine interim data analysis revealed a very serious problem with data in the study conducted by the other CRO that was not apparent in the i3 data set.

**Solution: Better rater and staff training.** By maximizing inter-rater reliability, the i3 CTA group can help to generate data that is sensitive enough to see drug effects if they truly exist. The rater training program for this study consisted of training at a series of investigator meetings and for new raters throughout the studies on the Mini Neuropsychiatric Interview, Panic and Anticipatory Anxiety Scale (a patient diary) and the Panic Disorder Severity Scale (a semi-structured interview). In addition to the didactic slide presentations, i3 produced patient interview videotapes for training and certification on the PDSS, as well as a videotape demonstrating how to instruct patients on filling out the diary.

i3 routinely conducts formal training on the psychometric and clinical properties of the scales being used, as well as specific therapeutic training on panic disorders for all internal i3 staff upon project award as well as periodically during the study. i3 considers this training essential to ensure that monitors understand the documents well and can be alert and proactive at the sites, as even well-trained raters can make errors. No similar training was provided to the other CRO staff.

**Result: Only positive study.** Some of the principle investigators in the other CRO's trial were making systematic errors in source documents used to extrapolate the primary efficacy measure. After the problem in the other trial came to light as a result of the interim data analysis, the CRAs from i3 were asked if they had seen this error in the i3 trials. It turned out that they had recognized a similar error early on in the study, but had successfully addressed the issue with their respective sites as a matter of routine. The superior training provided by the CTA group made a tremendous difference in the validity of the data collected — i3 CNS provided the only positive pivotal study. The trial conducted by the other CRO was not supportive and had to be repeated at great expense (and time) to the sponsor. The combination of i3's therapeutically focused CNS services and rater training enhanced the skills of the clinical team and quality of monitoring, and increased the chances of finding drug effects.