

CONDUCTING EARLY PHASE TRIALS IN SCHIZOPHRENIA

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It has always been difficult to find appropriate and adequate test subjects for clinical trials involving complex mental health issues such as schizophrenia. The FDA's stricter requirements for informed consent have made this challenge even more difficult.

"Informed consent is more than just a signature on a form," the FDA states in a recent communication to the industry. In fact, the agency regards informed consent as a process of information exchange that may include subject recruitment materials, verbal instructions, question/answer sessions, and measures of subject understanding. Furthermore, institutional review boards (IRBs), clinical investigators, and research sponsors are all listed by the FDA as responsible for ensuring the informed consent process is adequate. "Thus, rather than an endpoint, the consent document should be the basis for a meaningful exchange between the investigator and the subject," the agency adds.

I couldn't agree more.

SELECTING THE RIGHT PATIENTS FOR A TRIAL

When it comes to clinical trials involving people living with schizophrenia, proper patient selection is critical in the early phase program. Consequently, the site

investigative staff should have experience with schizophrenia trials. After all, schizophrenia is diagnosed based on clinical presentation; there are no diagnostic biological markers.

PRA's US sites are staffed by teams of investigators who execute innovative studies involving new drug candidates for the treatment of challenging psychiatric disorders. These specialized teams excel at conducting early phase projects, and are experts in psychiatric rating scales, rater training, and cognitive testing. This expertise ensures the demands of the FDA and the sponsor are fully met or exceeded.

Furthermore, a dedicated data services group supports each team, working to convert raw data into decision-point data for our clients. Sponsors and CROs can be confident that the reports they receive from our teams are comprehensive, and the raw electronic data are delivered in a format that is easily incorporated into internal systems for future analysis

A DEEP UNDERSTANDING OF THE PATIENT POPULATION

Remember, before a consent form can be signed, you need to address whether the patient has the capacity to give informed consent. Therefore, one of the foundations

of our success is a deep understanding of this unique patient population.

People with schizophrenia are far from being a monolithic group. Some patients need a certain amount of freedom during a clinical trial, especially a trial that lasts a month or more. For instance, they may need to leave the facility to handle routine chores.

Other patients are best managed with 24/7 care at one of our 200-bed facilities, however, they require flexible treatment, too. For example, many receive monthly benefits checks that are used to pay their rent. Our team often helps facilitate these kinds of tasks.

Our facilities are designed to look like welcoming hospitals. This is an important attribute with this patient population because making them comfortable and relaxed are critical components of ensuring a successful clinical trial.

There are even patients who need to be detoxed of all other drugs prior to starting a clinical trial. Therefore, it's important that each of these patient categories receives its own approach when conducting a trial.

PRA's well-vetted patient database — which includes more than 6,000 schizophrenia subjects — gives sponsors and CROs almost instant access to patients that

match their trial protocol. We have already conducted more than 200 schizophrenia studies, more than 35 Phase I trials, and nearly 150 in-patient psychiatric trials.

THE CHALLENGE OF INFORMED CONSENT

As stated earlier, the FDA's requirements for informed consent are complex. We share the agency's view that the consent process begins when a potential research subject is initially contacted. Although, under FDA regulations, an investigator may not recruit subjects to participate in a research study before the IRB reviews and approves the study. An investigator may only query potential subjects to determine if an adequate number of potentially eligible subjects is available. This can be a delicate time in a trial, and if handled improperly, it can result in a delayed or tainted clinical trial, which can expose a sponsor to lost money from a delayed market launch, or worse, create legal and financial problems if a trial goes seriously wrong.

This is why we're experts in navigating the complexities of the informed consent. We are also sensitive to FDA requirements in this arena. For example, when communicating with IRBs, we are clear as to who will conduct the consent interview. The IRB is also informed of when informed consent was obtained and if any waiting period (between informing the subject and obtaining the consent) will be observed.

As a psychiatrist, I feel strongly about doing our best to care for schizophrenics and their long-time suffering families. Therapy, buttressed by drugs and research, continue to make stimulating advances in treatment. Early stage clinical trials are one of the keys to maintaining this important momentum.



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David G. Krefetz, D.O., MBA, FAPA, FACN, CPI is a Medical Director for PRA Health Sciences Early Development Services in Marlton, NJ. Dr Krefetz has Board Certification in Psychiatry, Child and Adolescent Psychiatry and Administrative Psychiatry. He is a Certified Physician Investigator. In his role as Medical Director, Dr. Krefetz oversees all research studies and is part of the administrative team at Marlton.

From 2004 to present, Dr. Krefetz has served as a Principal Investigator as well as Sub-Investigator and Rater in pivotal clinical research trials. He has clinical experience working in a variety of settings including inpatient, outpatient, community and schools. He has a special clinical interest in disruptive behavior, mood, and anxiety disorders in youth, as well as with patients of all ages with HIV illness. He has conducted over 200 clinical research studies, including over 100 schizophrenia trials. He has been involved in schizophrenia research for 28 years.

Dr. Krefetz has authored over 20 clinical abstracts and posters and has been the author of research studies on ADHD, the evaluation of mood disorders in youth, as well as on the evaluation of depression and pain in persons with HIV illness.