VIEWPOINT

Network for Excellence in Neuroscience Clinical Trials
NeuroNEXT

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The US National Institute of Neurological Disorders and Stroke (NINDS) recently launched the first trial that will take advantage of the Network for Excellence in Neuroscience Clinical Trials (NeuroNEXT).[1-3] Through this initiative, the National Institutes of Health and NINDS hope to accelerate the progress of biomarker validation studies and therapeutic interventions through the phase 2 trial stage into clinical practice. NeuroNEXT consists of a Clinical Coordinating Center at Massachusetts General Hospital (request for application [RFA] NS-11-009), a Data Coordinating Center at University of Iowa (RFA NS-11-010), and 25 clinical sites throughout the United States (RFA NS-11-008). Academic and industry investigators studying neurologic diseases in children and adults can use this program by applying for grant funding while at the same time gaining access to the resources of NeuroNEXT. Small businesses may apply using the U44 Small Business Innovation in Clinical Trials (PAR-11-345) opportunity. Other institutions not associated with an institute of higher education may apply using the Infrastructure Resource Access (X01) (PAR-11-344). They will be using an agreement similar to that used by the National Cancer Institute to protect intellectual property of industry participants while testing their therapies. Foundations and advocacy groups also play an important role in study development through their partnership with NeuroNEXT. The NINDS has plans to dedicate $84 million over the next 7 years to alleviate the bottleneck of drugs in development for neurologic disorders.[3] This will decrease the burdens of cost and time, especially with the application of a central institutional review board to eliminate the need for institutional review board approval at each investigational site.

To be a successful applicant, a proposal will be required to incorporate the NeuroNEXT infrastructure into their proposed study. Ad hoc sites may be proposed to fulfill specific study requirements. Innovative and efficient study designs, such as adaptive designs and futility designs, should be used. The study population is intended to be patients, not healthy volunteers, and all trials proposing use of an investigational agent or device must have an active Investigational New Drug or Device Exemption. This opportunity is not intended to support the conduct of a clinical trial where the primary aim is to demonstrate efficacy or to support the conduct of a clinical trial to estimate intervention effect size for use in power calculations for a future phase 3 trial. The award and continuation of funding are subject to milestones.

During the application process, investigators will work with the Data Coordinating Center and Clinical Coordinating Center to determine the number of potentially eligible participants at the proposed sites. Once your protocol and timeline are finalized with the help of the coordinating centers, NeuroNEXT will assist with the study procedure manual and consent forms required. They will also assist with developing a data management and quality control system, developing study case report forms, and initiating contracts, start-up, and training of study personnel. Finally, NeuroNEXT will assist with completion of enrollment, follow-up of study participants, analysis of data, and submission of a paper for publication within 1 year of completion of all subjects' follow-up. They will provide public access to complete data within 18 months of study follow-up completion or after publication of the main study results article, whichever comes first. It is the principal investigator who is expected to contact the Food and Drug Administration to discuss further steps for establishing context of use of study-identified biomarkers when needed. As to the project timeline, the maximum request cannot exceed 5 years but the actual funded project period is dependent on reaching specific milestones.

This is not the first such NINDS network. It has previously launched successful multicenter research infrastructures including the Alzheimer's Disease Cooperative Study, Neuroprotection Exploratory Trials in Parkinson's Disease, and Neurological Emergencies Treatment Trials. The Alzheimer's Disease Cooperative Study has been particularly successful using the centralized model because it has initiated 30 research studies that were implemented at 20 or more centers, enrolling from 9 to 800 participants per study since its inception in 1991. They have helped to develop research and treatment centers for Alzheimer disease throughout the United States. Additionally, their studies have included those that developed the basic concepts and tools that we use to assess patients with Alzheimer disease as well as several drug trials.

The National Institutes of Health has used a similar infrastructure through other nonneurologic institutions including the National Institute on Drug Abuse Clinical Trials Network, who published a study evaluating the efficiency of this organization.[4] They found that the network approach decreased the time from last patient visit to database lock by 4.8 months, decreased database error rate, and reduced data management cost by 50%.

However, several details about the network are currently unclear and ought to be ironed out to prevent con-

fusion. In particular, the responsibilities of the principal investigator, the central sites, and clinical sites should be defined. For example, the Clinical Coordinating Center and Data Coordinating Center perform the data analysis, but it is not clear who has ownership of the data in terms of intellectual property and the ultimate responsibility of reporting the conclusions. Does the intellectual property remain with the principal investigator's institution or is it transferred to the National Institutes of Health or other sites? Does the principal investigator retain the final say in publishing the results and preparing the manuscript? Are other investigators at participating sites allowed to publish case reports/series of their own patients?

Monitors that oversee the conduct of the study and collection of the data play a key role in any trial that includes multiple institutions. Additionally, the lack of close oversight could potentially increase the risk of Health Insurance Portability and Accountability Act violations. It is unclear who will supervise the monitors and shoulder the associated costs of salaries and travel. Furthermore, in the event of injury or toxic reaction associated with a study, who will assume the responsibility of treatment or compensation to participants? Although the benefits of NeuroNEXT appear to far outweigh these potential problems, the solutions will need to be clearly defined early on in its inception.

ARTICLE INFORMATION

Published Online: August 5, 2013. doi:10.1001/jamaneurol.2013.3663.

Conflict of Interest Disclosures: None reported.

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