

Clinical Trial Site Start-Up

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In last month's column, we instituted the *Retina Specialist's Field Guide to Site Selection*, highlighting the importance of choosing the proper site for a productive retina clinical trial and outlining ways for sites to prepare and be selected for participation in an upcoming study. Sites that present themselves as efficient, productive, and experienced in the selection process place themselves in the best position to be picked by the study's sponsor. Likewise, understanding what is expected of your site is the first step toward completion of a study.

Now that your site has been selected to host a retina study, we will take a look at the clinical trial process from the perspective of an investigative site, targeting the certification process, the site initiation visit, and clinical pearls for conducting a successful study.

The study coordinator's (SC) role at a site is unique, and his or her importance cannot be overstated. We wanted to truly gain insight into site perspective, so we contacted two study coordinators who have extensive experience in the retina clinical trial field.

Mary Ann McCain, RN, serves as Clinical Research Manager (CRM) and SC at Tennessee Retina in Nashville, TN, after spending several years prior working with retina surgeons as a nurse in the OR. Tennessee Retina is one of the state's largest and most reputable retinal practices, with a staff of eight board-certified, fellowship-trained ophthalmologists, dedicated to the surgical and medical treatment of diseases associated with the retina, macula, and vitreous.

Jenny Daigle is an ophthalmic photographer, has previous retina SC experience, and is currently an Assistant Manager at Ora, Inc., in Andover, MA.

As discussed in our first column, the SC's duties frequently include correspondence with the managing parties and study subjects, maintaining study logs, and performing various clinical activities and data management.¹ Newly selected sites can benefit from McCain and Daigle's knowledge of critical site start-up information.

VISUAL ACUITY AND READING CENTER CERTIFICATIONS

Certification for retina clinical trials is not always an

easy process; it is often time-consuming and requires diligence and communication between the SC, site monitor, and the third-party certifying agency. Often sites are trying to become certified prior to the site initiation visit, which leaves SCs pressured to complete a number of labor-intensive certification processes. For purposes of standardization, consistency, and quality of data, clinical trial sites are often required to be certified for visual acuity (ETDRS) and reading center specifications, including fundus photography, fluorescein angiography, and optical coherence tomography (OCT) certifications.

The visual acuity certification process can be lengthy because both the lanes and the technicians themselves must be certified. This process may also cause scheduling conflicts with regular patient flow in a busy clinical practice. A third-party certification agency will frequently send a trainer to the site, and although the on-site training session is a critical component of the certification process, valuable clinic space, time, and personnel are made unavailable for up to a full day.

Fundus photography and OCT reading center certifications also require a similar significant time and effort commitment from prospective sites. Specific certification requirements may vary between reading centers, and images that must be captured during the certification process (and for the impending study, as is often the case) are often acquired in a different manner from images taken during regular clinical practice.

Further, photography certification (color stereo fundus photos and fluorescein angiography) can take several months depending on the skills of the photographer, the reading center's specific requirements, and the availability of appropriate patients. For example, if a patient cannot fixate well, the photographer may have a difficult time obtaining the necessary images. Similarly, in order to be certified to take photos, the photographer must understand the study's photography protocol and be able to achieve good quality photographs. As an ophthalmic photographer herself, Daigle recommends that photographers practice as often as possible. Although it is time-consuming and requires extra work, she says, it pays off in

the end to have a seamless understanding of the process.

Sites that have been previously involved in retina clinical trials and have already been certified in the aforementioned requirements, equipment and staff can often be grandfathered in for imminent clinical trials. If a particular site is a frequent participant in sponsored retina studies, has technicians that routinely submit images, or has worked with a particular sponsor before and has the appropriate documentation, recertification can sometimes be bypassed, thus facilitating a smoother and faster site start-up.

SITE INITIATION VISIT

The site initiation visit is conducted after the site has been selected by the sponsor to participate in the study, but just prior to when the site starts enrolling patients. This allows the sponsor or managing clinical research organization to conduct a detailed review of the study protocol with site staff and provide supplemental training as necessary; this process typically takes between 4 and 8 hours.² Topics of discussion may range from reporting adverse events and serious adverse events to protocol-specific inclusion/exclusion criteria and expectations for protocol compliance and deviation tracking. Before the visit, coordinate a convenient time for both your site and the monitor, and expect a pre-visit confirmation letter detailing the objectives of the visit.

The primary purpose of this exercise is twofold, for the benefit of both the sponsor and the site. It allows the sponsor to confirm that the retina clinical site has access to the required patient population, appropriately qualified staff, and adequate time and facilities to conduct the study,³ and it gives the site personnel an opportunity to become familiar with the clinical trial protocol. The monitor will verify that the investigational medicine product can be stored securely and that drug storage temperatures will be monitored appropriately. The monitor will also ensure that all necessary regulatory documents are up to date and stored in a well-organized binder. Sites preparing for an investigative visit would be well suited to review regulatory files for completeness, develop or utilize sponsor-generated checklists and/or source documents, ensure human investigation committee approval has been obtained or the review is in process, and if applicable, inventory supplies of case report forms and central lab supplies.

The monitor is likely to request time with the principal investigator (PI) in particular to discuss his or her responsibilities and to allow both parties to address any questions or concerns that may arise. Because the PI has a wide scope of responsibilities, he or she may choose to delegate these tasks to other staff members. McCain says that when they begin a study at Tennessee Retina, they hold a site kick-off meeting to make staff members

aware of the protocol and the tasks that must be completed. Although Tennessee Retina has designated clinical coordinators for each study, the staff employs an all-hands-on-deck approach to facilitate a smoothly run study. Additionally, the PI's approval of these task assignments should be captured on a delegation of authority log.

CLINICAL PEARLS FOR SUCCESS

Whether your site has a strong background in clinical research or you are new to the process, communication is key. Maintaining open communication lines between the sponsor and your site staff minimizes the risk of unnecessary complications. One way this can be accomplished is by ensuring that all parties know and understand their roles as the clinical trial progresses. Daigle recommends having applicable quick-reference guides available throughout the site to make it easy to outline how a certain task should be performed. For example, it is quicker to look at a reference guide for OCT submissions than it is to read through the entire manual, she said.

Hitting target goals, such as following the study protocol, providing the best patient care, and gathering accurate clinical data, all hinge around the working relationships developed during the conduct of a study. Additionally, smoothly run studies require good organization and attention to detail. McCain says that it is important to remind staff that the key focus should always be the patient. She says that because patients come to the practice every 2 weeks for some studies, they become familiar with and expect "red carpet treatment" on every visit.

In summary, the ideal site has a blend of therapeutic experience, flexibility, and excellent communication skills. Next month we will review other key factors for successful conduct of a trial. ■

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