The Retina Specialist's Field Guide to Site Selection

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Whereas clinical study protocol provides the scientific foundation for studies, an investigation's success may often be dependent on the collaborative efforts of the sites that participate. Therefore, proper site selection is fundamental in the facilitation of efficient, safe, informative, and timely clinical trials. If high-quality sites are selected—those that meet enrollment goals on time, implement the study protocol accurately and successfully, and are US Food and Drug Administration audit ready—the trial will likely finish on time, on budget, and provide viable clinical data to the study's sponsor.

How can you be sure that your site is ready to participate in an upcoming study? In this month's column you will discover what it takes to qualify as a site for clinical trials in retinal disease.

WHAT ARE CONTRACT RESEARCH ORGANIZATIONS OR PHARMACEUTICAL COMPANIES LOOKING FOR IN A SITE?

Generally, the parties managing clinical trials (eg, contract research organizations [CROs], pharmaceutical sponsors) are looking for sites with a proven track record in retinal trials. This track record includes familiarity, good understanding and adherence to Good Clinical Practice-International Conference on Harmonization guidelines, ability to enroll patients, complete study procedures, and maintain adequate and accurate study documentation, all to the highest quality, ethics, and efficiency standards. Specific CROs and pharmaceutical companies may have slightly different site selection requirements, depending on the company's individual management styles and the specific needs of the clinical trial in question. We, for example, evaluate sites involved in retinal trials based on three top criteria: capabilities, experience, and general excellence.

As you begin to think about your site for a clinical trial, it is important to remember that participation in a retinal clinical trial demands a major commitment. You can expect to invest time, staff, and facilities. Site participation also requires a sincere commitment to excellence and responsiveness from the site's investigators and study coordination team.

HOW TO BEST POSITION YOUR SITE ON PAPER

To present your site capabilities appropriately to potential CROs and study sponsors, you should know what will to be required of your location and how to articulate that information effectively. Most CROs and sponsors require completion of a feasibility or site qualification questionnaire or survey as an initial step in evaluating site prerequisites and the ability of sites to fulfill clinical trial stipulations. Historically, these questionnaires were in paper form, however, today's fast-paced electronic world may lead some CROs and sponsors to use Web-based questionnaires that allow them to tabulate responses quicker and acquire data faster. Do not be afraid to view either form as your site selection resume. Quite often, it may be the only tool available to you to convey information to the sponsor at this stage.

We cannot overstate the importance of being responsive. Although the questionnaires may seem like a tedious or trivial task, especially when you need to repeat the exercise for various sponsors, they are often the only tools for the sponsor to assess your site. The sponsor will rely fully on the site to conduct the study. On many occasions during the trial, the sponsor will need full cooperation and timely response to issues. Inherently, if a site is slow to respond to the feasibility questionnaire, it can make it difficult to include the site in the project.

When filling in the questionnaire, be accurate. Being truthful and thorough ensures that you are conveying accurate and realistic information about your office. Typical feasibility questionnaires include questions regarding satellite offices, doctors and investigators, common practice patterns, historical and current clinical trials conducted by the investigators, and experience with certain equipment (eg,

imaging tools such as spectral domain optical coherence tomography and high-resolution digital fundus photography systems) or experience interfacing with external resources such as central reading centers or laboratories. Other important topics might include whether you use a central or local institutional review board and the approval timelines associated with the agency, and whether or not your site has recently been audited by the FDA or other regulatory agency. This includes any critical findings that may have been listed on Form 483, issued when FDA investigators observe any significant objectionable conditions.

Make sure that your practice's assets are presented adequately. The two most important parameters are the patient population under your care and the research experience. If you have an experienced research coordinator at your site, for example, be sure to mention that. If you have a great track record hitting milestones on time, be sure to include this in your comments. Questionnaires may also be geared toward information on the volume and rate of visits for patients with specific retinal diseases who are seen at your practice. Access to local referral networks or patient communities may be of great value. Perhaps you have a recent radio or newspaper advertisement to attract new patients or maybe you have recently implemented a new patient referral system. This type of information can help the managing parties better evaluate your site and understand your capabilities.

If all goes well, and with notification from the managing party (typically via e-mail or a letter), you have successfully passed the first round of eliminations. Next up is the site qualification visit, where you will have the opportunity to present and establish your site, staff, and skills.

HOW TO SURVIVE A SITE QUALIFICATION VISIT AND SUCCEED

From the site's perspective, the outcome of the site qualification visit will likely determine whether or not the site will participate in the research. The sponsor and/or CRO may use the site qualification visit as a mode of ranking clinical sites to determine which are best suited for the current trial. The managing party will contact you to schedule a visit and may ask that you sign a confidentiality disclosure agreement prior to their visit. You should expect the visit to last 2 to 3 hours and be sure to schedule the appointment when potential investigators and key staff personnel will be available. This allows the facilitation between representative(s) and staff to run smoothly. It also helps to prepare for the visit by compiling investigators' CVs, licenses, accreditations of facilities, and associated laboratories, and confirming that all relevant diagnostic equipment is in working order.

Moreover, both the proposed principal investigator and the study coordinator should thoroughly review any materials provided by the managing party beforehand and prepare questions for the representative. If you have received even preliminary information on the study protocol, be sure to read it carefully and prepare accordingly. Although the representative may not be able to address every question fully, it is very important that you carefully consider your participation in the project and ensure it matches your practice and capabilities.

When the visit day arrives, show the representative around the facilities and the areas you would expect to use during the research trial. It may seem obvious, but ensuring that the office is neat and organized and that the staff is aware of the important visitors is common practice, and a good way to start off the qualification visit. Your evaluator is likely to interview the clinical research coordinator to assess his or her experience and availability, as well as the likeliness of forming and maintaining an open communication channel with him or her.[1] Some sponsors or CROs will likely return to visit your site during various stages of the clinical trial and will inevitably be in communication with you regarding progress, so look at your site qualification visit as a chance to establish a positive working relationship.

HOW IS THE DECISION MADE ABOUT WHICH SITES TO ENROLL?

The decision to take on an investigational site is not an easy one. The sponsor typically has no contact with the trial participants. Instead it is you, the site, that is responsible for conducting the study, so the sponsor must be able to place this vital project in your hands. Because opening sites in the study is expensive and time consuming, the sponsor is likely to engage the minimal number of sites that would guarantee a successful and timely project execution.

SIDEBAR

Common Mistakes

- Slow response to the questionnaires.
- Overstating recruitment and patient volume estimates.
- Failure to complete the feasibility questionnaire in its entirety (this provides the sponsor with partial information, making it difficult to include your site).
- Inadequate preparation for a site qualification visit.

Communication Pearls

- Be professional and accommodating to the needs of the sponsor or CRO representative.
- Respond promptly to feasibility questionnaires. Sponsors and CROs value quick turnaround, and it is often seen as an indicator of how responsive you would be during the course of the trial.

There are often some statistical considerations involved in the number of sites participating in a study. Managing parties will select the best and most suitable sites based on which centers demonstrate the best combination of infrastructure, capabilities, experience, recruitment prowess, and passion for excellence in clinical research. The CRO or sponsor will also need to know your commitments to other studies in order to assess the amount of time and effort that can be reasonably dedicated to the study at hand.

Conducting a successful clinical trial involves a large amount of paper work, coordination, responsiveness to changing schedules, patient interaction, and documentation. A typical busy physician will not have the time to dedicate to these tasks, and therefore it is critical to have a designated study coordinator. Some of the more prominent sites involved in retinal clinical research actually have dedicated study coordinators within research departments whose sole responsibilities are to conduct studies. Therefore, the responsibilities must be adequately outlined and transcribed so there is no confusion pertaining to individual and group roles.

USE YOUR RESOURCES

Finally, do not be afraid to contact the CRO or sponsor with any questions that you may have; CROs should make themselves available to you at all times to provide the best effort for accurate and meaningful data. If you need support, managing parties have the resources readily available to assist, so do not be afraid to ask. After all, once your site gains qualification for participation in the trial, it is truly in your best interest to maintain the qualities you have proven during the site qualification process throughout the entire trial. Not only does this ensure timeliness and accuracy in clinical trial results, but it also increases the likelihood of your site being selected to participate in future studies if the sponsor or CRO are impressed by your conduct.

It is our hope that this article will help sites gear-up for potential clinical trials. Stay tuned next month as we give you a glimpse at efforts driving the retinal science of the future when we look at clinical trials from the investigative site perspective. ■

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1. Woodin KE. Preparing for a study. In: Woodin KE (ed). *The CRC's Guide to Coordinating Clinical Research.* Boston: Thomson Healthcare, 2004.