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Common Challenges in Launching an Investigator-Initiated Multisite Study

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When an academic investigator does not have enough personnel or a large enough patient population at his or her site to successfully conduct a study, the investigator can enlist other sites to join the study. But, along with the contributions of all the sites, come significantly more complex regulatory, enrollment, compliance, operational and other challenges than faced by a single-site study.

For the lead investigator, multisite studies are a world apart from a single-site study or as one site in a multisite, industry-sponsored study. Launching a multisite study is like putting together a 1,000-piece jigsaw puzzle with moving parts, knowing that some of the pieces will be wrong and some will be missing.

The first thing a lead investigator must do at the beginning of a study is to assemble a capable team and develop a realistic, comprehensive plan that addresses all the issues raised by a multisite study. Lead investigators often rely on a coordinating center to help address the issues and to operationalize their efforts. The issues addressed by a coordinating center can include site diversity, standard policies and procedures, whether to use a single IRB, and how to develop a study budget. In contrast to a clinical research organization (CRO), a coordinating center plays more of a supporting and advisory role.

Here are some of the issues a lead investigator faces:

Site Diversity

The lead investigator must understand that every site has different policies, procedures, personnel, organizations, etc. What works at the lead investigator's site probably will not always work at every other site and maybe at none of them.

For example, a lead investigator with a large research team must understand that investigators with smaller teams may not have the same level of backup personnel for holidays and vacations. A lead investigator at an institution with an active quality monitoring program must understand that some institutions, without much exaggeration, think quality assurance means making sure all the informed consent forms have been signed. A lead investigator in the center of a large city may not understand the population accessible to an investigator in a small city across the country.

Standard Policies and Procedures

Different sites have different policies and procedures. In some cases, that will not be a problem for the study, but in other cases standardization will be required.

Create a set of documents that explain how the study will operate, such as a Manual of Procedures (MOP) and a Patient Recruitment Plan, setting forth the roles and expectations of the coordinating center and the sites. Update the documentation based on questions that come in and any regulatory changes.

Single IRB (sIRB)

The National Institutes of Health (NIH) now requires all sites in a federally funded multisite study to use a single IRB. Because this mandate is relatively recent, do not assume that all sites in the study will be familiar with the sIRB process or the study IRB's policies, procedures, technology, etc. After working out the details with the study IRB, perhaps in consultation with a few of the planned site IRBs, each site must sign a "reliance agreement" saying that it will rely on the study IRB for ethical review.

Some of these IRBs may not have much experience with the sIRB model or may disagree with the study IRB on certain policies or procedures, so explanation and possibly negotiation may be required.

Also keep in mind that just because a study is being overseen by a single IRB, it doesn't mean that sites don't have to adhere to their own site policies. Individual sites will still be expected to submit an initial review of their own at their site. Informed consent becomes more complicated as most studies will have a master consent and each site will also have their own local context portion of the ICF that lays out their participant compensation and other local policies. This can create real challenges when it comes to version control, but if an Investigator is expecting them, safeguards can be put in place to ease the burden on the study as a whole.

Study Budget

Developing the study budget for a single site can challenging. Developing the budget for a multisite study is even more challenging because additional activities are required and sites vary. Unexpected costs often arise in connection with the sIRB model, startup, training, site initiation, laboratory, medical monitoring, data safety and monitoring board, site management, and every other aspect of the study.

Protocol amendments, case report form revisions, technology glitches, personnel changes, site replacement, test article supply, and other issues can create unexpected costs.

Conclusion

Dealing with the above challenges can give a lead investigator new respect for the study teams at biopharma and medical device companies and CROs.

Too many clinical studies of all varieties run off the rails because inexperience, pressing deadlines, an overabundance of enthusiasm, or insufficient risk assessment and management cause studies to advance prematurely from planning to execution.

Advice from an experienced lead investigator can help. If the study is funded by a drug or device company, their expertise may be available. A professional coordinating center can provide valuable expertise, experienced professionals, established processes, and relationships with proven vendors to deal with the above challenges.

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