

APPLIED CLINICAL TRIALS

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YOUR PEER-REVIEWED GUIDE TO GLOBAL CLINICAL TRIALS MANAGEMENT

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Avoiding the 5 Common Mistakes at Study Startup



Study sponsors often face budget and time constraints during study startup which can lead to poor decisions that ultimately will affect the study long after the startup phase. Based on my experience managing studies in the pharmaceutical and CRO industry I have identified five common

mistakes sponsors can make during study startup, and how these mistakes can be avoided:

1. Not starting with a final protocol

Having a final protocol before you begin the startup process is one of the most important requirements for a successful clinical trial. You can begin many startup procedures with a draft protocol, but it is risky to begin collecting regulatory documents (1572, financial disclosure, etc) until you are sure the protocol title is final. If a protocol title changes after materials are distributed to the sites, everything has to change. This results in significant added costs and delays as well as very frustrated study coordinators.

Additionally, we always have a final IRB approved protocol prior to the investigator meeting. Being organized and having the final protocol for your investigator meeting can help ensure that you make a lasting, positive impression on your sites and you can begin screening subjects immediately after the meeting. Studies always enroll faster if the study sites can begin screening after the meeting rather than waiting weeks for a revised protocol. If you need investigator feedback on your protocol get it well before the meeting. You can even hold a teleconference with your top five investigators and get everyone's feedback at the same time. This is an area where your CRO can help by working with you to finalize the protocol before your initial investigator meeting.

2. Not having sites initiated in a timely manner

A delay of more than two weeks between your investigator meeting and when you begin screening can have a negative effect on recruitment and enrollment. You can avoid expensive recruitment challenges and delays by making sure that your sites are ready to begin screening for your study immediately after the investigator meeting. Doing so enables you to capture and build on the investigator team's excitement and knowledge gained at the meeting, and it makes them eager to work on your study. I would rather reschedule an investigator meeting than hold it and risk a delayed start. It will always cost money in the end if a study is delayed following the meeting.

I advise using the investigator meeting as the initiation visit rather than conducting a separate visit if the PI/Subl and coordinator both attend the meeting. It is only necessary to hold in-person initiation visits if one or both didn't attend the meeting. You also want to give higher priority to the sites that attend the meeting to begin screening subjects after the meeting. If you have a large study (more than 50 sites) and every site needs an initiation visit before allowed to screen subjects this will delay your start. It's almost impossible to conduct 50 initiation visits in two weeks.

3. Underestimating timelines

It's important to allow enough time for vendors providing services like EDC development or drug packaging and shipping to prepare for a new study. There is no EDC system that is without problems. If you start a study with your EDC platform fully in place you will prevent a backlog of study data entry and you'll know about any problems with the system early on. Most EDC systems take 10 to 12 weeks to get up and running. You can do it faster, but that creates a risk that you will face problems with the queries or something else in the middle of the study that causes more work for the site. You want the system live and fully functional at the investigator meeting. If you train sites on a template system you risk not knowing the problems with the system until well into the study.

Sponsors also want to take as much time as they need to conduct the site selection process. Every site should go through a pre-study visit whether it's via phone or in-person. If you worked with a site previously, conduct a phone pre-study visit. Never assume that a site is able to enroll or complete a study until you've interviewed them extensively. If you allow enough time you can thoroughly evaluate every site and ask the right questions.

Another important item is to have the drug ready to ship upon request. It is a mistake to start a study that doesn't have the drug packaged and ready to ship to a site.

In the long run it makes it easier for sponsors to attract the best sites because they will develop a reputation for being organized with their studies. You don't want to be the sponsor that has a reputation for never being ready or prepared at the investigator meeting.

4. Poor CRF design and not implementing full, correct UAT (User Acceptance Testing)

Spend quality time making sure that your CRF design and/or setup of your EDC system are accurate and thoroughly tested. Give yourself enough time to conduct UAT and system checks. Correct UAT means testing the system at least three times as well as having the CRAs and several sites review it, because they really know how to look at data.

You want to be sure to have proper testing from all different areas including CRAs, the site, data management, etc. You want to push the system in every possible scenario as possible. Remember the workload for the coordinator when you are creating multiple screens and setting up queries. A coordinator doesn't want to enter data into four pages just for the demographic info. Try to put as much info on the same screen as possible. This makes life easy for the sites.

A simple CRF can quickly turn into a big problem in the middle of the study if you underestimated the database setup and design at startup.

5. Not having "Plan B" or C and D in place for slow recruitment

Good site selection early on can ensure that you have enough sites and that they have a sufficient patient pool to cover enrollment, including anticipated dropout rates. Prepare and educate your project team on the

recruitment challenges they may anticipate.

Some common recruitment mistakes:

- Selecting sites that are high prescribers of the marketed version of the product. Just because a doctor prescribes the medication doesn't mean they can enroll patients into an "investigational" study for that same indication.
- Filling your study with opinion leaders. Being experts on the protocol does not necessarily make them experts on how to recruit patients for a study.
- Assuming all selected sites will enroll patients. You should anticipate at least 10% will not even get IRB approval before the study is complete. Always have a list of back-up sites that have IRB approval and are ready to go at a moments notice.
- Underestimating the total number of sites needed for a study. Although less sites are easier to manage, more sites will ensure enrollment timelines are met. The cost savings with fewer sites will outweigh the costs to extend your study if you experience recruitment delays.

Listen to your sites during site selection. If more than 25% tell you it will be difficult to enroll or the protocol is difficult to follow, you need to prepare early for the problems. Ignoring the warning signs doesn't make them go away.

Offer concrete solutions for addressing recruitment needs throughout the study. It's a good idea to have a "Plan B" strategy for slow recruitment in place before the study begins so you can quickly take action as soon as you see the problem. Plan B can be adding more sites within the first 30 days if enrollment is not what you anticipated, or changing the advertising strategy.

As clinical trials and study protocols become increasingly complex it's essential that sponsors and CROs work together to guarantee that clinical studies use the best strategies and tactics to run smoothly, from startup to closeout.

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