



The Study Budget

An Important Aspect of Clinical Trial Site Success

Developing a site budget specifically for an individual study demands the same careful analysis as review of the study protocol.

Producing a sound budget is a major responsibility for any principal investigator (PI). Just as accurate budgeting contributes to a sponsor's success in bringing a product to market, financial accountability is a significant factor in the success of every individual clinical trial site. It is therefore vital to ascertain that budgetary expertise is not ignored during the initial planning stage for the study. Developing a site budget specifically for an individual study demands the same careful analysis as review of the study protocol. Creation and supervision of this financial tool is a necessary function of the PI, but is rarely addressed in the formal medical and regulatory training that brings an individual to his or her role in research.

Many platforms exist for the performance of clinical research. These include full-time, freestanding research centers, university-based research sites, and individual or group private practice settings. The following will outline a decision-making process from the perspective of a private practice setting, but will refer whenever possible to the other venues.

The Prelude

Communication and accord between the PI and sponsor are needed to achieve a smooth operation throughout all aspects of the planned study. Glitches and bumps can be anticipated, and means of potential resolution mutually accepted, so as to ensure the efficient progress of the trial.

First, one must determine accountability. If the PI is new to the budget planning process, consideration must be given to finding a credible assistant with specific training, expertise, and experience in building clinical trial budgets. Ultimately, however, decisions should rest with the PI.

Next, the study protocol is reviewed in detail with the entire study team. The team's involvement aids in identifying challenges unique to the responsibilities of each department. All sub-investigators, coordinators, assistants, laboratory, regulatory, and financial staff will have input. It is humbling to discover how often individual staff members perceives their particular part in the project very differently from the way the investigator sees it. In a recent "easy" study, it was only after enrolling the sixth patient that a meaningful, budget-impacting error was identified. Laboratory work required by the phlebotomist and coordinator exceeded the time allotted; the resulting additional costs reached significant proportions once calculated for each patient's required serial lab studies. The budget was significantly exceeded.

The Process

Several popular methods can be used to construct a budget. “Bottom-up,” “target,” and “historical” are a few. In the “bottom-up” approach, the PI assigns an hourly wage for each team member’s time. The time spent for each line item is then recorded to determine the number of hours devoted to each specific activity by each individual. This is then multiplied by the estimated hourly wage for each individual participating in this specific activity. The sums obtained for each individual activity are then added up to derive the final cost of this part of the trial. Specific activities assigned to each section of the project are then added to each other to arrive at the final charges for the clinical trial.

The “target” budget model is used by many in our field. This system utilizes expectation as its basis. The PI determines that a particular sum, i.e., \$400–700, is the average expense per visit per patient, regardless of what procedures or amount of time is involved in a particular protocol. Then, he or she multiplies the number of visits by the particular average sum selected to determine if the budget will likely suffice for the benefit of the site and the sponsor.

The “historical” approach relies on experience and the availability of previous budgets applied to similar studies. A budget is put together in line-item format and compared with that of the previous study to determine if it seems satisfactory to all concerned.

Another means of presenting a budget to a site is predicated on a sponsor-prepared per-visit reimbursement without specific identification of the individual procedures that comprise the visit. In this instance, the investigator should assume the responsibility to break down the budget to a fee-for-service format. In this way, the reimbursement can be evaluated as commensurate with tasks and time spent.

More complex protocols may run into an issue when a particular study procedure is skipped or forgotten. This can lead to an uncomfortable situation when the sponsor balks at paying 100%

for the visit. Only very simple, straightforward studies should adopt this type of budget.

Important Considerations

A few qualifying comments should be noted when utilizing the “bottom-up” system. This method of creating a budget requires special concentration on “non-fixed costs” or time-related activities. Examples of these instances are found in informed consent discussions with participants, recruiting and screening efforts, completion of essential case report forms by the coordinator, and careful review of laboratory results, diaries, and data transfer by the investigator.

Any compromising of the time estimates allotted to routine tasks in the interest of cost savings should be avoided. Misguided attempts to stay within inadequate budget estimates could lead to serious adverse events or missed warning signals, and ultimately to distorted outcomes and disastrous consequences. The complexities and individual issues pertaining to each study must be thoughtfully considered as worst case scenarios, and anticipated as potential expenses.

Sponsors may spend a significant amount of money on central advertising, only to find it is not helpful in recruiting.

As an example, a frequently underestimated line item is the informed consent discussion. Proper and complete discussion often takes 30–60 minutes, sometimes longer. There is a huge difference in the time needed for various means of obtaining consent. Only a few minutes may be consumed when the goal is simply obtaining a dated signature at the bottom of a form assumed to have been read by the patient. On the other hand, an hour or more may be needed, or even more than one visit,

when the goal of the staff attendant is to document that the participant understands clearly each line of a forthright, well-written informational explanation of the goals, methods, limitations, and risks pertaining to the experimental procedure.

Many other issues routinely confronted in creating a budget need to be individually recognized (see Table 1 for a summary):

A startup fee is often overlooked by both investigators and sponsors. This is a nonrefundable charge that is paid up front to the site; it is distinct from advance payments (see below). This fee, charged by the site, includes time for reviewing the protocol, the investigator’s brochure, and the budget itself. Also routinely forgotten is the time spent reviewing charts and study protocol with appropriate individuals and sections of clinic staff. Not all sponsors view this time as a compensable expense unless the PI explains and documents these meetings.

Advance payments are an occasional source of confusion because they may be disguised or “lost” as part of startup fees. These up-front payments for the first one or two patients enrolled reflect that these patients will serve as instructional models to establish routines for future enrollees. The payments are deducted from later payments that have been made at scheduled intervals, and therefore are primarily a means to help generate early cash flow. Most sponsors offer advance payments, but it is important to separate them from startup fees, as they are two entirely distinct items.

Advertising grants should be negotiated as a separate line item. It is helpful to learn from sponsors how they intend to approach study marketing. Some sponsors expect enrollment from the site’s patient databases. They do not intend to subsidize recruitment. Others will set up a central advertising campaign, or will consider a local, site-specific form of promotion.

Experienced sites learn and decide which form of publicity, centralized or site-specific, works best for them. They can then recommend, in writing, the best method to promote recruitment for their site. Sponsors may spend a significant

TABLE 1. Issues Routinely Confronted in Creating a Budget

Startup fees	Negotiate for time spent setting up and organizing trial
Advance payments	One or two patients is the standard
Advertising grants	Negotiate specific to individual study demands
Payment schedule	Pay attention to milestones and hold sponsor to them
Holdbacks	Standard is 10–20%
Screen failures	Negotiate based on past experience and trial complexity
Overhead expenses	Standard is 20–30%, but is trial specific
Miscellaneous	Don't forget dry ice, storage, IATA, and IRB fees

amount of money on central advertising, only to find it is not helpful in recruiting. The sponsor is then reluctant to allocate extra dollars for site-specific advertisements. Although not reported as often, the reverse could also be true.

Be aware of how site-specific advertising will be paid. Most sponsors ask that you put out monies first and then invoice for reimbursement. This rationale is easy to understand: The site is expected to be more familiar with local media. The issue of recruitment advertising is closely related to early cash flow, so do not ignore it. Some sponsors allocate funds up front for this advertising, making cash outlay easier on the site.

The payment schedule is an often overlooked feature of the budget. Sponsors generally pay on a monthly or quarterly basis. Occasionally, for a particular trial, payment will be based on certain milestone criteria. The importance of the payment schedule cannot be overemphasized. The site's financial staff needs to remain aware of and alert to all payment issues in a timely manner. Based on enrollment, screening, or randomization visits, monitors are required to come to the site to verify data. They will submit data to the sponsor on behalf of the site. The site must be ready with follow-up to the appropriate sponsor personnel in order to verify that payment has been sent. It is very helpful to include in the contract a request that all payments from sponsor to site be accompanied by a spreadsheet defining what the sponsor is paying for with each particular payment. It is not uncommon to receive a check in the mail identifying the study, but not indicating for which patient or procedure the check has been issued.

Holdbacks, amounting to 10–20% of the total contract, are standard for most trials. The sponsor will pay 80–90% of the total contract, with the remainder to be paid at data lockout after study closure. Remember, if you were an early enroller in a multicenter study, you may have to wait many months for all other sites to close out before receiving your last (holdback) payment. Anticipate this in your cash flow planning as you finalize and settle your site expenses.

Screen failures (SFs) are also a very negotiable line item. It is difficult to predict the percentage of patients that will fail screenings. Neither the site nor the investigator should be penalized for legitimate SFs (i.e., for those identified by laboratory or imaging studies).

Sponsors usually allow payments for a mutually agreed upon percentage of patients enrolled. For example, if you agree to a 25% screen failure rate and you have enrolled 12 patients, you are entitled to be paid for three screen failures. As some studies evolve, and a significantly higher than agreed-upon SF rate occurs, reintroduce SF rates for discussion with the sponsor. Sponsors walk a fine line here by encouraging enrollment, but being unwilling to support a high SF rate. A high SF rate may indicate protocol issues.

Overhead expenses should be written into the budget and are routinely accepted by sponsors. The accepted percentage usually ranges from 20% to 30% of the total contract, is site specific, and is determined by the type of existing overhead. University sites generally have a higher overhead due to higher fixed costs and a bureaucratic organizational structure; private sites are expected to incur lower fixed overhead costs.

Miscellaneous line items are trial specific and will become apparent as the study progresses. You will want to add a few to most budgets:

- *Dry ice* is often difficult to obtain and should be a line item if called for in the protocol. Check your lab manual and meet with your lab staff to learn if dry ice is needed.
- *Chart storage* may be required for up to 15 years, adding a costly line item. Sponsors may balk at this. However, they may also accept the charts and binders for storage.
- *International Air Transportation Association (IATA) certification* for coordinators may be required for some clinical trials. This is a certification for shipping and handling dangerous substances. The site may be responsible for individual staff training in management of hazardous substances, or the sponsor may help fund this training.
- *Institutional review board (IRB) fees* can affect cash flow to the site. Most central IRB fees are paid directly by the sponsor, and the site is not involved at all. Occasionally, the site is asked to pay this fee up front and then invoice the sponsor for reimbursement. Sites that utilize a local IRB usually pay the fees themselves and invoice the sponsor for reimbursement.

In summary, the effort the clinical trial site puts into budget analysis may be time consuming and tedious, but eventually will separate a financially successful study from one that loses money. The latter may “make or break” the viability of an otherwise entirely capable investigative site. Do not hesitate to obtain the best trained personnel and put their financial expertise to work in this extremely important endeavor. **ACRP**

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