A New Paradigm in Clinical Trial Budgeting

Legal requirements for sponsors have mandated new processes in clinical trial budget development. Have research sites adjusted?

Clinical research sites continue to struggle with managing their economic reality. Recent data indicate that many clinical research sites are not operating on a financial break-even basis. A primary concern for many sites managing this financial situation is the inability to negotiate a fair study budget. Frustration over trial budget negotiation is not a new challenge; however, the tenor of sponsor negotiation has dramatically changed over the last several years. This article reviews recent study budget regulations and the corresponding effects on the budget negotiation process.

A Series of Unfortunate Trends

Clinical research is performed in a myriad of platforms, including free-standing research centers, university-based sites, and private practice settings. All of these clinical research organizations rely upon revenue generated from clinical trials to fund their operations. This situation obviates the need for effective study budget development.

Over the long term, research sites that are unable to conduct accurate budget analyses and negotiation will lose money. Economic concerns are compounded by the fact that nearly two-thirds of all clinical research studies are placed in community-based, for-profit sites. Private practices are unable and unwilling to sustain unprofitable, nonessential endeavors. Stated simply, successful research budget negotiation is required to ensure the viability of clinical research programs.

Recent data indicate that financial pressures are having a devastating effect on investigators. A study published in 2006 analyzing principal investigators conducting U.S. Food and Drug Administration (FDA) and National Institutes of Health (NIH) clinical trials reported several illustrative results. Only 65% of the investigators conducted a trial in the previous year; only 10% participated in research annually over a five-year period. There is a small core of active investigators, and a turnover of about 40% of the rest. Further, the rate at which investigators permanently terminate their research has doubled. The Tufts Center for the Study of Drug Development reports that the number of principal investigators conducting industry-sponsored trials has declined by 11% since 2001. The entire research industry may suffer from a lack of experienced clinical research investigators without a new system of budget development.
Clinical research site managers have often voiced frustration with the study budget process. Nationwide, site managers feel that budgets are decreasing while the resources required to implement new protocols are increasing, and clinical trials are growing more sophisticated to meet regulatory needs. As a result, the number of unique procedures per subject increased by 33% from 2001–03 to 2004–06. Phase IIIb/IV trials have witnessed the greatest increase of protocol procedures: 45%.5

Unfortunately, sponsors have not provided a corresponding increase in funding of these research activities. From 2000 to 2005, the price that sponsors pay research sites per subject for Phase II/III studies increased by 42%. During the same period, the complexity of these clinical studies, as measured by the total number of procedures performed, increased 49%. In inflation-adjusted dollars, the price per procedure decreased by 15.6%.6

Principal investigators, site managers, and coordinators have the task of analyzing and negotiating the budget for their institutions. This is a challenging process for both sponsor and site professionals. Parties on both sides are met with confusing language, an inability to communicate, and unfortunate stereotypes. According to industry statistics, unsuccessful contract/budget negotiation is a top reason for site initiation delay.7 Frustrated site managers have often concluded a sponsor negotiation hearing “let me talk to my manager.” Sites may not understand that recent regulatory limitations have modified the negotiation process.

Recent Regulations Have Redefined the Negotiation Process

Clinical research site professionals receiving the “let me talk to my manager” statement may conclude that sponsors are unwilling to provide adequate funding for studies. This unfortunate assumption makes it seem that the sponsor is using its stock-market short-term earnings statements to provide economic growth to shareholders, at the expense of the principal investigators. Recent federal regulations have completely changed this paradigm.

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The Office of Inspector General (OIG) in the U.S. Department of Health and Human Services has published a set of federal regulations that has dramatically affected the process of clinical trial budgeting. In the last several years, the OIG has issued compliance program guidance directed at the healthcare industry that is intended to manage fraud and other financial abuses. On April 18, 2003, the OIG issued a regulatory document titled “Compliance Program Guidance for Pharmaceutical Manufacturers.”8 Although it may have missed the attention of many sites, this document has resulted in a reformation of research budgeting.

The OIG compliance guidance provides a direct mandate to sponsors concerning research budgeting. Funding for research projects to physicians must be transparent and documented. In fact, the regulation states that “payments for research services should be fair market value for legitimate, reasonable, and necessary services.” Sponsors must be careful in ensuring that they are paying investigators only for services rendered in direct support of a research protocol.

In addition to a new focus on cautious budgeting, a secondary federal regulation requires that all funding to investigators be detailed and documented. The Federal Register states that payment of these types is a criminal offense unless the remuneration is set in writing and documents the purpose of the funding. Moreover, the clinical trial budget must cover “all of the services” included, and specify “the services to be provided.”9 Sponsors are absolutely required to implement these regulations; noncompliance is an illegal and costly error.

The combination of these two regulations has elicited a powerful response from the pharmaceutical and medical device industry. The pharmaceutical trade organization, PhRMA, published a document titled “Principles of Conduct of Clinical Trials,” which was revised in June 2004 and states that payment to investigators should be based on work performed. This guidance document further requires that “a written contract for budgetary agreement should be in place, specifying the nature of the research services to be provided and the basis for payment for those services.”10 The medical device organization, AdvaMed, issued a document with several similarities. Revised in April 2005, the AdvaMed “Code of Ethics on Interactions with Healthcare Professionals” addresses funding for clinical research, and states that clinical trial budgets must be consistent with fair market value and “specify all services to be provided.”11

The described federal regulations and corresponding industry guidance have resulted in a new focus on conservative clinical trial budgeting practices. Most trial sponsors have a legal department to ensure compliance with these new requirements. Site managers should not despair, however, because this legal intervention does not necessitate smaller budgets. In fact, most sponsors realize that there is a relationship between properly funded sites and their contribution to a trial. Sponsors remain motivated to expeditiously complete research trials. A single day’s delay in bringing a drug to market can cost $1.3 million dollars.12 This is compounded by the increasing number of trials; statistics indicate that between 2001 and 2003, the number of FDA-approved drug studies rose from 3,900 to 4,500.13 Sponsors are interested in providing appropriate financial support to sites that can assist them in completing research trials.
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The world of research budgeting has evolved over the last three to five years. Research sponsors are not cheap; they are legally required to be careful. In the most simplistic terms, budgets are no longer managed by accountants; they are controlled by industry lawyers. The lawyers develop the budgets in preparation for legal justification; as such, they are motivated to assign a conservative and defendable financial value for every clinical procedure and project activity. Successful research sites will recognize this new reality and prepare for a different type of budget negotiation.

Site Budget Methodology—New Tools for Success

An article in the October 2007 Monitor included examples of “bottom-up,” “target,” and “historical” budgeting processes. With respect to the new regulatory requirements, only a detailed quantitative cost analysis will provide the research site with the information it needs to negotiate a fair study budget. Sponsors will respond to this detailed information, but it is the site’s responsibility to justify any additional budget requests. A documented, detailed, quantitative cost analysis represents the foundation of any successful negotiation. Any site can produce a detailed cost analysis by following these three steps:

1. Analyze project implementation costs
2. Document indirect costs
3. Develop and present a detailed cost-analysis report

Analyze Project Implementation Costs

The first step in developing a detailed cost analysis is identification of all resources required to directly support the clinical trial project. Divide the resources needed to run the trial into two separate categories: protocol- and project-based costs.

- Protocol-based costs include the time, effort, and purchased services required to conduct every protocol visit.
- Project-based costs include all other resources needed to efficiently implement this medical research project.

The sponsor needs to provide funding for all protocol- and project-based expenses.

Start the quantitative cost analysis by analyzing the protocol-based expenses. This is the most intuitive budgeting activity; in fact, many sponsors are fairly accurate in proposing adequate funding for conducting study visits. The site must answer two basic questions for every study visit: What supplies or services must be purchased? How much time is required to complete the visit? The answers to these questions must be determined and converted to financial figures. A simple example of this process is presented in Figure 1; this protocol visit will require coordinator and investigator time, purchased services from two external business partners, and a subject stipend for a total cost of $317.50.

Analysis of project-based costs is intended to identify all nonvisit activities associated with conducting the trial. One article stated that 75–90% of the time that a site spends on a study is not in the budget as a direct cost; it is spent on the dozens of hidden costs. Sites need to understand their hidden project-based costs. One strategy is to write down a list of anticipated project-based activities when opening a study, managing the project, and closing a trial. Figure 2 contains an example of one site’s template for reviewing the project-based costs during study initiation. This example includes 30 line-item activities that are common to any clinical trial. The process of analyzing these data indicates that the startup fee for this study should be $3,188.50.

In order to negotiate funds for various project-based costs, some research sites have begun charging sponsors a standard startup fee. For example, many sites are requesting a $2,500 startup charge. Such nonspecific charges should be discouraged. The use of unjustified fees indicates that the site has not analyzed the workload associated with the trial. Some studies have a higher level of administrative or project-based work, and no two studies are identical. In order to ensure the site is not forgoing the opportunity to request the appropriate amount of funds, all studies should be analyzed individually. One single specialty site

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Figure 1 Sample Protocol-Based Cost Analysis*

<table>
<thead>
<tr>
<th>Activity</th>
<th>Resource</th>
<th>Time (Hours)</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Coordinator</td>
<td>2.00</td>
<td>$100.00</td>
</tr>
<tr>
<td></td>
<td>e-CRF Entry and Documentation</td>
<td>1.50</td>
<td>$75.00</td>
</tr>
<tr>
<td></td>
<td>Laboratory Services</td>
<td></td>
<td>$30.00</td>
</tr>
<tr>
<td></td>
<td>Patient Stipend</td>
<td></td>
<td>$25.00</td>
</tr>
<tr>
<td></td>
<td>Physician Exam</td>
<td>0.25</td>
<td>$37.50</td>
</tr>
<tr>
<td></td>
<td>Radiology Services</td>
<td></td>
<td>$50.00</td>
</tr>
<tr>
<td></td>
<td><strong>Total Cost</strong></td>
<td><strong>$317.50</strong></td>
<td></td>
</tr>
</tbody>
</table>

*Report generated by IntelliTRIAL™ research management software.
that analyzes these fees requesting between $1,800 and $13,000 for startup fees. A detailed and customized review of project-based costs will ensure the research site is fully compensated. It is unrealistic to expect sponsors to include the site’s hidden costs in a budget when many sites ignore them or cannot detail them to the sponsor.14

Document Indirect Costs

The concept of quantifying indirect costs is a challenge for many research sites. Depending on the organization, a sponsor may or may not be charged for many types of indirect or overhead costs. The specific overhead value can be difficult to compute; sites may need to involve their respective corporate controller or accountant to determine the appropriate overhead rate. Calculation of indirect costs should include consideration of the following cost types: building, rent, utilities, depreciation, general supplies, uniforms, waste handling, and personnel support from information technology, medical records, human resources, business office, and management representatives. Sponsors understand that the research site may need to provide financial support for these indirect costs; however, a lack of a consistent overhead policy between sites renders this a confusing item for sponsors. Approximately 50% of sites are required to provide funding for a portion of indirect costs, but the coverage pattern and financial result are variable between sites. A research site should determine its own overhead rate and utilize this value in budgeting for all clinical trials.

Develop a Detailed Cost-Analysis Report

The final step in producing a detailed quantitative cost analysis is the development of a report that clearly describes all of the previously identified direct and indirect expenses. In order to negotiate a fair budget, the site must be able to provide the sponsor with a complete report documenting all cost types and expected expenses. In most cases, the sponsor will provide each site with its boilerplate study budget. This budget proposal represents the sponsor’s understanding of a site’s protocol implementation expenses. Every site operates in a very different expense environment; thus, every study budget should be different. The detailed cost-analysis report will provide a foundation for transparent and objective budget negotiation. Additionally, a site-specific cost report will eliminate the longstanding one-budget-fits-all debate.

The detailed trial cost-analysis report must be comprehensive and intuitive and must include justification for the entire study budget. The federal regulations require the sponsor to contract with the site and specify all services provided. A detailed cost-analysis report must provide this information. To aide negotiation, the cost-analysis report should include a comparison to the sponsor’s budget proposal. Figure 3 includes an example of study expenses compared to the sponsor’s budget.

A presentation at this level of cost granularity and comparison to the budget proposal will assist the sponsor’s legal representative in justifying a budget increase for the site. The involvement of legal professionals in the negotiation process requires more upfront work from the site; however, it may reduce the feeling that the sponsor is trying to withhold funding.
new legal policies are designed to ensure compliance with federal regulations; sites can utilize these policies their benefit. A well-developed justification of study expenses is difficult to deny. In summary, the sponsor may require rationalization and documentation of budget requests; however, this demand requires the sponsor to respond to all expenses a site presents.

The process of identifying expenses and developing a detailed cost-analysis report may seem overwhelming to many research professionals. The clinical trial management software industry is already responding to this new paradigm of budgeting; several products contain financial wizards that can complete all of the calculations discussed in this article within 10–15 minutes.

**Conclusion**

Clinical research sites continue to struggle with financial pressures. In order to ensure the viability of their research, sites need to develop enhanced budget negotiation practices. Federal regulations and industry guidance require sponsors to actively manage the clinical trial budget process. Sites that intend to make budget requests are required to justify their demands. To negotiate an appropriate budget, sites need to conduct a detailed and quantitative cost analysis on every trial. Sites and sponsors must realize that the paradigm of study budget development and negotiation has evolved from “let me talk to my manager” to “this will have to go through legal review.”

**References**


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