



Clinical Trial Budgeting

Financial Issues

In this lesson, we describe the financial processes and issues that arise in clinical trials. The lesson begins with some perspective on where budgets fit into the clinical trial process, to listing and describing cost components, and then providing strategies on budget negotiation and cost recovery. A checklist and section with common terms and phrases associated with financial aspects of clinical trials are found at the end of this Lesson.

This Lesson will focus on two alternative funding sources: industry or the federal government. Each sponsor has its own particular issues and concerns.

Importance of Budgeting for Industry Sponsored Trials

Without a properly negotiated and prepared budget, the investigator and the institution will lose money on a clinical trial. Because a clinical trial contract is a fixed-price agreement, the investigator is obligated to perform the work described in the contract, even if the actual costs exceed the total contracted amount.

The sponsor may initially quote a budget amount allocated to each site, or may ask the investigator to develop a budget for review. In the case of a sponsor-determined budget, the quoted amount may be adequate or generous, but this is often not the case.

In most cases, a reasonable compromise can be reached after performing a cost analysis and reporting those calculated costs to the sponsor. However, on occasion it may be necessary for the investigator to turn down a clinical trial because of an inadequate budget offer. Equally important are the terms of the payment schedule. Consider when payments should happen and whether it makes sense with the timing of procedures in the study.

Importance of Budgeting for Federally Funded Trials

Federal guidelines are very specific about fees and costs that may be included in study budgets. Up-to-date information about the price of hospital services is also required. Therefore below are a few items to address early in the process.

Items to Address before Beginning Budget Development

- Can the investigator recruit subjects?
- Does the budget support the work to be performed?
If the investigator cannot answer yes to each of these questions – then decline the trial
- Find the study overview in the protocol. This is often a one page visit-by-visit outline of the study
- Determine if the labs and testing procedures such as ECG's (electrocardiograms), MRI scans (magnetic resonance imaging), etc. will be analyzed in a local lab or at the sponsor's site
- Determine if there will be professional charges required for the technical tests performed. An example would be an ECG with interpretation by a Cardiologist
- Either edit the sponsor's budget or create a spreadsheet to reflect all costs of the trial
- Negotiate a cost per subject to complete a clinical trial, not a cost per test or procedure
- It is permissible to use a standard of care test result for clinical research
- It is not permissible to bill insurance for a test, device, or service paid for by the sponsor
- For multi-year trials, consider adding an inflation rate to the per-completed-subject cost
- If you will be the coordinating center for multi-site studies, assess differences in local research patient care fees and coverage decisions/regulations.

Now that some of the issues have been brought out into the open for discussion it is time to move to the information gathering step.

Who Pays for What and Why: Gathering Expense Information

Clinical trial budgets are usually quoted to the sponsor based on an amount per patient enrolled. To determine what amount to request, prepare a line-item budget for the salary of the personnel involved, the supplies, the testing to be performed, and other costs of the work plus Facilities & Administrative (F&A) costs also known as indirect costs. We will use these terms interchangeably. Then divide the total estimated cost by the anticipated number of patients. In addition, it is common for start-up costs to be incurred regardless of the number of patients. For example university Institutional Review Board (IRB) review fees for company protocols must be charged to the sponsor, but are not included in the per patient costs.

Common Expenses

Clinical Activities

Obtain research (see note below) and regular rates for:

- Each clinical procedure
- Standard of care vs. clinical trial cost
- Out patient clinic room
- Laboratory fees
- Central lab
- Overnight shipping

- Pharmacy charges
- In patient room
- Radiology
- Office and clinical supplies

Note: Generally a research hospital or academic medical center will have a “regular” rate for services or procedures, but will frequently provide a discounted rate for “research.”

Personnel (including fringe benefits)

Estimate time and effort in the form of a percentage of effort. Academic medical centers allocate effort based upon a percentage of an individual’s full time effort. The benefit of this methodology is to eliminate the difficulty in expressing full time effort in hours worked per week, which could range from 40 to 65 to 100 hours per week. A consistency is created by expressing effort as a percentage. When expressing effort worked think of the percentage of time (versus total work time) the individual spends on the clinical trial for example over a one week or one month period.

- Physician
- Coordinator
- Technical
- Clerical

Subject Payment (whether or not subject continues in a study)

Define amounts and times for:

- Per visit stipends
- Travel
- Meals
- Parking
- Publication Costs

One Time Costs

- IRB Review Fee (Ranges vary by institution and region. For-profit IRBs publish their rates, which could be used as a general guide.)
- IRB Continuing Review Fee
- IRB Amendment Review
- IRB Preparation Fee
- Investigational Drug (IND) Pharmacy set-up fee and storage costs
- Archive document storage fee \$rate / year for 7 years
- Source document binders per patient
- Advertising for recruitment

Administrative Costs

Obtain rates and/or amounts for:

- Facility & Administrative (F&A) costs also referred to as indirect costs, are costs that are

incurred by a grantee for common or joint objectives and cannot be identified specifically with a particular project or contract. Facility & Administrative (F&A) costs and the phrase indirect costs can be used interchangeably. Most universities classify their clinical trials for F&A purposes as “off-campus research,” which for federal sponsors is capped by A-21 at 25%. For commercial sponsors many are charging their actual administrative costs, many of which are in the mid 30s.

- Cancellation Fee if sponsor terminates study. This provides the institution with some recovery of “sunk costs” in starting and running a trial.

It is not unusual to negotiate with sponsors who may resist paying the institutionally approved (F&A) indirect cost rate. Treat the rate as non-negotiable. Provide detailed, line-item cost for each activity; be prepared. Use phrases such as, “The full cost of participating in the clinical trial is...”

If your institution is providing subcontracts to numerous sites from a federal award, the subcontractors should be permitted to assess their full F&A rate.

Less Common Expenses

Just completed was a presentation on some of the more common expenses of a clinical trial. The following is a list of less common expenses, but these should also be built into a budget if the intent is to recover the full cost of a clinical trial.

Startup Time

All trials require a significant amount of time before enrollment actually begins. Consider time spent doing the following:

- Site selection visit
- In servicing staff
- Investigator meeting
- Setting up services with other departments
- Site initiation visit
- Source document creation
- Regulatory documents
- Informed Consent Form (and translation costs for the benefit of subjects for whom English is not their first language)

Protocol Requirements

Translate the activity into a measure of time. For example, the schedule of events may list that vital signs are to be taken at each visit. How long does it take to complete a set of vital signs? Also, keep in mind the time required to draw blood.

How long does a difficult blood draw take? How long will it take to process and package the specimen? If telephone calls need to be made, estimate the time required. Consider worst-case situations. Also

consider the time spent doing the following:

- Recruiting
- Explaining administration of a drug
- Screening
- Review of diaries
- Consenting
- Protocol specific procedures
- Taking a history
- Conducting a physical exam
- Explaining the activities of the protocol
- Pharmacy set up and dispensing

Day-to-Day Operations

The trial will require time outside of the protocol. Calculate the time spent actually running the trial. Include:

- Communication with the sponsor/CRO
- Maintaining the study file
- Case Report Form completion
- Monitor visits
- Faxing documents
- Resolving queries
- Reporting Serious Adverse Events

How do we handle a situation when the Sponsor provides the budget?

Clinical trial sponsors usually provide a budget for a study and often require this budget to be included in the contract. Sponsor budgets should be reviewed carefully, in conjunction with the study protocol. Sponsor budgets should always be compared against an internal budget to insure that all study costs are included. Since it is usually necessary to negotiate aspects of the budget, the investigator should view the initial sponsor budget as a draft, revising it as necessary.

Payment Schedules

Sponsors will usually specify certain milestones that must be achieved before payment is made. Pay close attention to the timing and requirements of the milestones. Payment schedules may be appended to the contract as a table or may be written as a paragraph within the contract.

Please see below for an example of a common payment schedule for a trial with 10 patients at \$2500/subject.

PAYMENT	MILESTONE	AMOUNT
1	Initial Payment upon drug shipment	\$2500

2	After 3 subjects completed	\$7500
3	After 2 subjects completed	\$5000
4	After 2 subjects completed	\$5000
5	Final payment after all Case Report Forms are completed, queries are resolved and close out visit is complete	\$5000

A preferred payment schedule would be:

PAYMENT	MILESTONE	AMOUNT
1	Initial Payment + IRB fee upon contract execution	\$6500
2	After 3 subjects randomized	\$7500
3	After 2 subjects completed	\$5000
4	After 2 subjects completed	\$5000
5	Final payment after all Case Report Forms are completed, queries are resolved and close-out visit is complete	\$2500

Occasionally, initial payment will not be sent until a subject is randomized. This situation is not acceptable. If a subject is never randomized, no payment will be received and costs have been incurred that will not be reimbursed. Instead, ask for a reasonable initial payment that will cover startup costs. This amount should be adequate to cover all costs incurred with initiating a trial including the IRB fee in the event that the trial never begins.

Look at the milestone payment. Will payment be made upon completion of Case Report Forms (CRF's)? That may mean waiting until the monitor has reviewed the CRF's and sent them into data management. Will payment be on completion of a subject's participation in the trial? This may delay payments. An ideal schedule will reimburse after a reasonable amount of subjects have randomized or after a certain number of visits are completed so that the study account does not run a deficit.

Sponsors may also choose to hold back a significant portion of payment until all study activities are complete. Ensure that this is not an excessive amount. 10% of the total budget would be ideal. Final payment may or may not depend upon waiting until all sites are closed or until the database has been closed. Pay close attention to this because it can mean that final payments may be delayed for an unreasonable amount of time.

An ideal payment schedule would include the following:

- Non-refundable initial payment that includes IRB fee and startup costs
- Regular payments with realistic milestones
- Final payment made upon closure at site
- Invoicing permitted for other costs (i.e. equipment, advertising)

- Whenever possible, attempt to negotiate an advance payment from sponsor to cover trial start-up and to help cash flow.
- Specify how soon the payments are due following each deliverable milestone (e.g., thirty (30) days).

Screen Failures and Early Termination

Not every subject enrolled in a trial will complete the trial. Ensure that the budget and payment schedule provide for these circumstances adequately.

It is difficult to cover every issue regarding a clinical trial, but the above presentation covers a significant portion. In closing, the following are a few more issues to consider.

Issues to consider

- Charge effort to a non-federal account until the study is approved. The federal government does not want to support an industry supported clinical trial.
- Deal carefully with professional fees when using time and effort in percentages (be careful that these costs are not duplicated, if company is covering professional fees then be sure Medicare is not reimbursing as well)
- When costing out the expenses, the clinical trial will probably have a mix of study patients in the study population - some with Medicare and some without. Determine which costs are covered by Medicare, insurance or the clinical trial.
- Qualifying trial – This term is used to denote that Medicare coverage of specific clinical trials explicitly authorizes [Medicare] payment for routine patient care costs and costs due to medical complications associated with participation in clinical trials.
- QV modifier required (Medicare qualifying clinical trial coding and billing). Be sure those who are involved in coding and billing fully understand the complex set of Medicare requirements; avoid double billing.
- Be aware of a possible conflict of interest with the investigator if an existing relationship exists with the funding company, especially a consulting or financial relationship. Be sure a conflict of interest policy is established and disclosure forms are current. It is important that all conflicts of interest are administratively managed in order to avoid the appearance of bias.

Conclusion

A successful clinical trial will include a budget that adequately meets the financial needs of conducting a trial. Since costs vary across the nation for supplies and services, budgets are almost always negotiable.

Sponsors usually use one of two options when presenting a budget. Sponsors may offer a certain amount per patient and ask that the investigator work within that amount or the sponsor may ask to formulate a budget of estimated expenses. Regardless, it is the responsibility of the investigator to ensure that the amount agreed upon will adequately cover all costs associated with conducting a

clinical trial.

Please note that retrospective research, data registries, etc. do not meet the clinical trial definition and therefore are not eligible.

Typically, Facility & Administrative (F&A) costs --referred to as indirect costs-- are not waived for industry sponsors. To do so would force the institution to subsidize the performance of industry sponsored research with institution dollars, a generally undesirable situation.

Ensure that all fees (except the IRB fee) include F&A costs. This includes General Clinical Research Center fees and all invoiced costs such as MRI's, EKG's, advertising, etc. For example, the sponsor will reimburse the investigator \$1,000 for an MRI required by the protocol. Divide the total amount by 1.00 + the F&A rate to determine the amount available to pay the fee after F&A rate is applied. (e.g. $\$1,000/1.25 = \800 available to pay the MRI fee).

Checklist

Subject Costs

- Cost per subject x Maximum number of subjects
- Cost per screened subject x Maximum number of screened, but not enrolled
- Cost per dropped subject x Maximum number of dropped subjects
- Bonus x Number of subjects qualifying (This is an incentive payment to the institution, not to a subject or members of the investigative team.)

Study Charges Up Front Costs

- IRB fee
- Capital equipment (include cost of maintenance if applicable)
- Sub-contracts
- Record storage charges
- Informed consent form translation
- Advertisement(s)
- Special supplies
- Training costs
- Source document preparation

Management Charges

- Pharmacy charges (storage and preparation of drug)
- Monitor visits (Coordinator time)
- Post-study Coordinator charges
- Protocol amendments
- Physician fee (Salary and benefits)
- Coordinator fee (Salary and benefits)
- Administrative Assistant fee
- Technical fee

- Research Administrator

Administrative Charges

- Facilities & Administrative (F&A) costs also known as indirect costs

Common Financial Terms and Phrases Used in Clinical Trials

F & A

Facilities and Administrative Costs are costs associated with general operation of an institution that cannot be precisely allocated to a project. May include operations and maintenance, general administration and departmental expenses and libraries. F&A costs are differentiated from direct costs. Also commonly known as indirect costs.

Fringe benefits - Allowable as part of overall compensation to employees in proportion to the amount of time or effort employees devote to the grant-supported project, provided such costs are incurred under formally established and consistently applied policies of the organization

Institutional Review Board (IRB) fee

It is the policy of most academic medical centers to charge a sponsor a flat fee for every trial that is reviewed by the IRB. This is a one-time fee that covers the initial application, amendments, renewals, SAE reporting, etc. The IRB fee is not subject to F&A costs.

Investigational Drug Service

When evaluating the budget, remember that all investigational drugs must be stored and dispensed from the Investigational Drug Services pharmacy. Fees vary depending upon the type of trial being conducted. It is expected that the pharmacy fees will be included in the budget. The pharmacy fee is exempt from F&A at some institutions, so be sure to determine what the policy is at your institution. Please be sure you understand the fee structure especially when you are negotiating this part of the budget.

Personnel costs and fringe benefits

Institutional base salary - The annual compensation paid by an organization for an employee's appointment, whether that individual's time is spent on research, teaching, patient care, or other activities. Base salary excludes any income that an individual is permitted to earn outside of duties for the applicant/grantee organization. Base salary may not be increased as a result of replacing organizational salary funds with grant or contract funds. Compensation costs are allowable to the extent that they are reasonable, conform to the established policy of the organization consistently applied regardless of the source of funds, and reflect no more than the percentage of time actually devoted to the project.

Professional fees - Disposition of Professional Fees

Fees resulting from clinical practice, professional consultation, or other comparable activities performed pursuant to the purpose of the award must be assigned to the sponsoring institution for disposition in accordance with established organizational policy. The term “professional fees” does not apply to honoraria, fees for scholarly writing, delivery of occasional outside lectures, or service in an advisory capacity to public or private non-profit organizations, which, if permitted by organizational policy, may be retained by the fellow.

Time and effort

Personnel - Individuals who contribute to the execution of a project in a substantive, measurable way. Carefully examine the budget for the time requirements. Most protocols include a "schedule of events" which breaks down all study tasks required by the protocol.

Case Study

Now that roles and responsibilities have been determined, IRB approval has been obtained, and the research team has met to discuss the study protocol, Dr. Expert considers the finances of the trial. She knows that she will incur expenses in order to conduct the clinical trial but does not know where to begin or how to develop a budget. She contacts the departmental administrator Ms. Doitall to ask for help. Ms. Doitall also brings in the expertise of Mr. Ino Grantz who can help build a budget to cover the projected costs of doing the clinical trial.

Again, this will be a small Phase II clinical trial sponsored by a pharmaceutical firm called CuresAll, Inc. Dr. Expert believes she can recruit 20 or more patients who will qualify to participate in this study.

Mr. Grantz uses his knowledge and experience to discuss potential costs with Dr. Expert. Along with the departmental administrator, Ms. Doitall, Dr. Expert works up a realistic budget that would cover the costs of doing the clinical trial. Frequently the central contracts and grant administration office has to be consulted in order to determine costs such as IRB fees and Facility & Administrative costs. During the discussion with Dr. Expert the list below represents potential expenses that need to be budgeted to determine the cost per patient in order to determine how much in Total Costs to ask the sponsor, CuresAll, Inc.

One time costs:

- Initial IRB fee - \$1,500
- Budget and contract negotiation fee - \$1,200

Management costs:

- Principal Investigator (PI) oversight – 1 hour per patient, 20 patients, \$200 per hour
- Study management – 30 hours at \$50 per hour

Study Costs (Clinical Trial)

Costs) Site Visits

- Initial Site Visit – 16 hours at \$50 per hour
- Preparation for Site Visit – 4 hours at \$50 per hour
- Time Spent with Site Visitor (5 hours/day times 2 days) at \$50 per hour
- Total of 9 site visits not including the initial site visit
- Study Closeout Activities – 12 hours at \$50 per hour

Patient Recruitment

- Patient Identification - 0.5 hr per week for first year at \$50 per hour
- Patient Screening - 0.5 hr for estimated 50 patients at \$50 per hour

Patient Visits

Patient Consent at \$50 per hour

- Prepare Consent Paperwork Packet - .25 hour
- Inform Patient – .75 hour
- Obtain Appropriate Signatures and Copy for File - .50 hour
- Randomize Patient and Complete Paperwork - .75 hour
- Update of Study Spreadsheets - .50 hour

Baseline Visit at \$50 per hour

- Prepare for Visit - .50 hour
- Interview with Patient - .75 hour
- Form Completion and Filing - .50 hour
- Update of Study Spreadsheets - .25 hour
- Preparation for Surgery - .50 hour
- Securing and Binding Films - .50 hour
- Sending Films and/or Forms – 1.0 hour
- Surgery/Hospital Information – 1.0 hour
- Query Resolution - .50 hour

6 week Post-Operative at \$50 per hour

- Prepare for Visit –
- Interview with Patient –
- Form Completion and Filing –
- Update of Study Spreadsheets –
- Patient Follow-Up –
- Securing and Binding Films –
- Sending Films and/or Forms and Invoicing –
- Query Resolution -

3 Month Post-Operative – 4.25 hours at \$50 per hour

6 Month Post-Operative – 4.25 hours at \$50 per hour
12 Month Post-Operative – 4.25 hours at \$50 per hour
24 Month Post-Operative – 4.25 hours at \$50 per hour
Biennial Visit – 4.25 hours at \$50 per hour

Indirect Cost Rate (Facilities & Administrative Costs, F&A) – 25%

Pretend that you are Mr. Grantz and Ms. Doitall, and that you must complete a clinical study proposed budget. Please use the Excel worksheet entitled “Clinical Research Budget Case Study” which is provided. Some hints: Be sure to fill-in the cell for the number of patients and the rate per hour so that the cell formulas work properly; and the cost per patient should come out to \$3,262.50. Good luck!