Financial Oversight of a Clinical Trial

Institutions need to be cognizant of particular costing standards that indicate what cost can and cannot be charged to a trial, including methodologies for cost allocations. The trial site’s objective is to create a budget that includes reasonable estimates of all costs expected to be incurred, compliant with the costing standards applicable to the trial site.

Even if care is applied during the budgeting process to ensure a clinical trial will be financially self-sustaining, the trial could experience a deficit unless disciplined oversight is provided during the life of the trial.

Billing errors could occur without proper oversight which could also result in compliance issues. Clinical trial billing errors can have negative consequences for both the institution (which can have fines and penalties and suffer harm to reputation) and to the physician (who can be vulnerable to civil and criminal penalties, including jail time).

Examples of billing errors are:

- Services that are not standard of care being billed to insurance
- Services whose costs are a component of the sponsor’s per participant reimbursement amount yet also billed to insurance (Double billing).

Due to the inherent complexity of clinical trials, their budgets are unique and difficult to predict and manage. A trial budget changes constantly, much like the clinical trial itself.

What is driving my financials through the roof?

Costs are driven by many factors, and when these factors change, so will your budget. Here are a couple of the top cost drivers to blame for trial budget increases:

1) **Protocol amendments** – Changes to the study design can result in significant rework and increase costs. Additions such as additional tests, increase in overnight hospital visits and increases in patient monitoring.

2) **Timeline delays** – Many budgetary elements of a trial are driven by duration. Extending a trial timeline is not just spreading remaining costs over a larger period of time, it is an increase in resources, staff time and salary, research pricing, is not guaranteed for the life of the study and therefore an increase in the trial expenses without negotiating an increase in budget.

3) **Changing study personnel** – There are differences in salaries for study personnel and these changes can impact the bottom line.

It is almost universal that the financial management of a trial is the most painful aspect and requires a team to maintain. The PI and study coordinator need to understand the protocol, then to enter data into the software of record timely and meet with accounting on an adequate schedule. Accounting needs to understand the milestones, invoiceables, and restriction (travel, equipment, etc.).
When the study is approved to start!

PI, study coordinator(s) and accounting need to have a kick-off meeting to review the budget and billing requirements (template). Having an understanding of what was agreed to before work starts, will be very helpful as the trial starts enrolling patients. This meeting will also establish who is responsible for getting the calendar in On-Core set up (CTSI), then to confirm with Fairview/UMP/M Health that the research rates quoted are still valid and get purchase orders in place where possible, enter study data and review invoices.

The AHC and the CTSI On-Core staff are available to help and on their website (www.ctsi.umn.edu) is a list of required data to be entered.

Maintaining Participant – Level Cost Information

Maintaining participant-level cost information is a prevention control with regards to billing errors. This involves creation of a grid whereby each column corresponds to procedures, items or tests conducted chronologically throughout the life of the trial, for which the sponsor will pay the cost.

The grid needs to include columns to record time spent by the clinical trial team members during the life of the trial that is not a component of the procedure fee which the sponsor needs to reimburse (e.g., time to complete case report forms).

Each row of the grid is assigned to a participant enrolled in the study (de-identified). As the study participant completes each visit and undergoes each procedure, the respective date is entered onto a grad in the appropriate column on the participant’s row. The AHC has assigned a timeline of 72 hours from the appointment to entry into On-Core/TASCS.

This grid can be used by the finance professional to monitor revenue earned and billable items, as well as effort for all trial team members.

EFFORT

The percentages of effort allocated to all of the individual’s activities must reasonably reflect how the individual spends his/her time. Effort of a clinical trial team member for a single participant encounter might be de minimis, yet be measurable in the aggregate over the life of the trial. An approach is needed to ensure a reasonable approximation of effort is reflected in the clinical trial’s general ledger account as the time occurred. If there is trial activity, effort should be allocated to the trial account.

There is a higher inherent effort reporting risk with clinical trials that have a larger participant enrollment targets versus clinical trials with smaller enrollment targets. Higher enrollment equates to increased variability of clinical team member effort amounts. ON-Core/TASCS uses the calendar/grid to track.
ONGOING REVIEW AND RECONCILIATION

A timely reconciliation of costs anticipated to be reflected in the clinical trial’s account compared to transactions that are actually recorded is a detection control.

There are two general categories of costs that need tracking in a clinical trial – participant specific and non-participant specific costs.

   a) Participant Specific
      During the life of a trial, bills for services are received (from Fairview, UMP, M Health, Anesthesia, etc.) that indicate the study participant’s name, procedure, date and cost incurred. The study coordinator needs to compare these bills against the information on the participant grid (see above) to determine if the pricing methodology is compliant.

   b) Non-Participant Specific
      A detail of costs associated with activities that are not participant specific should be maintained. The detail should be updated based on encumbrances and time reporting of clinical trial members. On a schedule, these items need to be compared to the original budget and adjusted as needed.

Maintaining a detail of protocol costs incurred is a prevention control to ensure the trial site is aware of when a billing milestone is achieved and a bill is to be sent to the sponsor. Such a detail also serves as a detection control when payments originate with the sponsor (such as reimbursement for submission of case report forms).

Accuracy of the grid is paramount to support the billing of milestones.

Tools Available

The tools that are available for study monitoring may require training and approval to access.

NOGA (Notice of Grant Award)

The NOGA is presented by SPA to the PI and the Research office for the PI. The NOGA is a cumulative report summarizing basic award information, key award terms and conditions and budget information. The information in the NOGA is cumulative and will display from inception through the end of the project period. This can be re-run from EFS Reporting.
UMReports – The best report for reviewing revenue is the ‘Sponsored Award Overview’, by using the CON# you get the full report with Primary project and any child accounts. In the upper right hand corner of the report is a line; Open AR Amount ITD 0.00.

If the space 0.00 is highlighted and underlines (as above) then you can click on the 0.00 and get the most current revenue that has been billed to the sponsor and/or has been paid.

This trial started 2/1/15 and enrollment is open until 1/31/2018. This is the start-up costs, no patients enrolled (9/16).

EFS- PeopleSoft Enterprise Financial System

The PeopleSoft Enterprise Financial System is the single main source of all financial data at the University. All Revenue, and Expenses current and future are maintained in EFS. SFR (Sponsored Financial Reporting) uses the data from EFS to generate their invoices and reports required by the sponsor.
Spectrum Program

The University offers many courses for the team members (PI, Study Coordinator, DRA) involved in research. Descriptions of the courses and registration for these can be accessed for ULearn under Research Education.

Ready! Set! GO!!

The PI and study coordinator have received what they need to get started now as the DRA (Department Research Associate) accountant or analyst you need to gather information what you need.
Clinical Trial Definitions

Ancillary Services: Those special hospital services for which charges are customarily made in addition to routine services. Ancillary services include x-ray, operating room, laboratory, pharmacy, blood bank, and pathology.

Billing/Contract Milestone: The point at which a study site is entitled to reimbursement for services under a fixed fee contract. The milestones are written into the contract, including the amount of reimbursement. For the purposes of clinical research, milestones are generally in the form of case report forms.

Blinding: A set of procedures that prevent study participants, caregivers, or outcome assessors from knowing which intervention was received by a study participant. A study can be either:

Single Blind: A study design in which one party, either the investigator or the study participant is unaware of what medication the study subject is taking.

Double Blind: A study design in which NEITHER the study participants nor the investigator knows which study participants are receiving the experimental drug and which is receiving a placebo (or another therapy).

Case Report Form: A printed, optical, or electronic document designed to record all the protocol-required information of a study participant that must be reported to the sponsor.

Category A Device: An innovative medical or health-related device for which absolute risk of the device type has not been established (e.g., initial questions of safety and effectiveness have not been resolved and the Food and Drug Administration (FDA) is unsure whether the device type is safe and effective).

Category B Device: A non-experimental and/or investigational medical or health-related device where the incremental risk is the primary question (e.g., underlying questions of safety and effectiveness of the device type have been resolved), or it is known that the device type can be safe and effective because, for example, other manufacturers have obtained FDA approval for that type of device.

Charge Master: A list of current rates for inpatient services, ancillary services and professional fees.

Clinical Research: Research that either directly involves a particular person or group of people or uses materials from humans, such as their behavior or samples of their tissue. (The process of clinical research protects personal data).
**Clinical Research Coordinator (CRC):** The person at the study site that is responsible for conducting clinical trials using good clinical practice (GCP) to the extent consistent with FDA and the Department of Health and Human Services (DHHS) regulations and guidelines under the supervision of the Principal Investigator (PI).

**Clinical Trial:** A type of clinical research involving human subjects, designed to provide results regarding the safety and efficacy of a health-related drug, diagnostic, device or procedure.

**Clinical Trial Budget:** A detailed spreadsheet showing all events associated with a study, including the institutional cost and amount charged to, or negotiated with, the sponsored. A clinical trial budget is developed for each research study to assess the financial feasibility of the study.

**Clinical Trial Monitoring:** The person employed by the sponsor or a contract research organization that is responsible for determining that a trial is being conducted in accordance with the protocol. A monitor’s duties may include, but are not limited to, helping to plan and initiate a trial, assessing the conduct of a trial, and assisting in data analysis, interpretation, and extrapolation. Monitors work with the CRC to verify completeness of all data and documentation from the trial in conformity with the protocol, standard operating procedures, GCP and applicable regulatory requirements.

**Code of Federal Regulations (CRF):** The codification of the general and permanent rules published in the Federal Register by the executive departments and agencies of the federal government. It is divided into fifty titles that represent broad areas subject to federal regulation.

**Clinical Trial Agreement:** Document containing the terms of an agreement between a sponsor and the institute for conducting a clinical trial. The contract should identify whether the study is sponsor initiated or investigator initiated, name the parties to the agreement, PI responsible for the conduct of the clinical trial and include the study protocol and study budget and information regarding the items and services for which the sponsor is paying.

**Confidentiality Agreement:** A confidentiality agreement (CDA) is an agreement by any two parties restricting the distribution, use, dissemination or other non-authorized use of the confidential information in any form. CDA’s are also known as secrecy agreements, non-disclosure agreements, or letters of confidentiality.

**Conflict of Interest Disclosure:** The process through which a clinical trial team member formally notifies his or her employer of personal financial interests (including those of his/her spouse and dependent children) which are (or could be perceived to be) a conflict of interest. Any disclosed apparent conflict must be managed or eliminated prior to the initiation of a clinical trial. Also referred to as an outside interest. Also see financial definition.
**Contract Research Organization (CRO):** A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor’s clinical trial related duties and functions.

**Cooperative Agreements:** A large network of researchers, physicians, and health care professionals at public and private institutions throughout the US, Canada and Europe. Sponsored by the National Cancer Institute (NCI) these groups work together to promote and design clinical trials of new cancer treatments.

**Coordinating Center:** The primary site for a multicenter trial that facilitates communication and provides direction and payment to all participating sites, including collection of all study data.

**Coordinating Investigator:** An investigator with the responsibility for the coordination at different site participating in a multicenter trial.

**Current Procedural Terminology (CPT) Codes:** Numbers that are assigned to every task and service a medical practitioner may provide to a patient including medical, surgical and diagnostic services. All providers use the same codes for the same task or service, thus the CPT Codes ensure uniformity.

**Efficacy:** The maximum ability of a drug or treatment to produce a result regardless of dosage. A drug passes efficacy trials if it is effective at the dose tested and against the illness for which it is prescribed.

**Effort:** Reporting: A process through which an individual certifies that his or her compensation was properly charged for all work activities (including sponsored activities such as clinical trials) in percentages reasonably reflective of time devoted to each activity. This process is utilized to comply with federal cost principles at academic institutions which receive federal funding.

**FDA Form 1572 (Statement of Investigator):** The document used by the FDA to identify qualified investigators to participate in clinical investigations. By signing the form, the investigator certifies that he/she will comply with all FDA regulations.

**Facilities & Administration Costs:** See Indirect Cost definition.

**Federal Cognizant Agency:** The Federal agency that awarded the greatest amount of direct awards to an awardee or contractor based on the expenditures reported in the awardee’s/contractors annual independent audit report.

**Financial Disclosure:** The process by which a clinical trial team member certifies to the absence of certain financial interests or to disclose those financial interests. Also see Conflict of Interest definition.
**Good Clinical Practice (GCP):** A standard for the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity and confidentiality of the study participants are protected.

**Good Laboratory Practice (GLP):** A quality system concerned with the organizational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported.

**Human Subjects:** Defined in Code of Federal Regulations [21 CFR 50.3] as an “individual who is or becomes a participant in research, either as a recipients of the test article or as a control. A subject may be either a healthy human or a patient”. A human subject is often referred to as a “study participant”.

**Indirect Costs:** Costs that are incurred for common or joint objectives and therefore, cannot be identified readily and specifically with a particular sponsored project, or any other institutional activity.

**Informed Consent:** A document by which a study participant voluntarily confirms his or her willingness to participate in a particular trial, after having been debriefed of all aspects of the trial that are relevant to the study participant’s decision to participate. The informed consent document includes a description of the participant’s financial obligations and identifies the items and services, if any, that will be provided at no cost to the participant. It also describes the clinical trial’s purpose, objective, investigational products, procedures, risks, benefits, and relevant contacts.

**Informed Consent Process:** The informed consent process involves giving a human subject adequate information concerning the study, providing adequate opportunity for the human subject to consider all options, responding to the human subject’s questions, ensuring that the human subject understands the information, obtaining the subject’s voluntary agreement to participate and, continuing to provide information as the human subject or situation requires. To be effective, the process should provide ample opportunity for the investigator and the human subject to exchange information and ask questions.

**Institutional Review Board (IRB):** An independent body comprised of medical, scientific, and non-scientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial. Among other things, the IRB reviews, approves, and provides continuing review of a clinical trial protocol and the methods and materials to be used in obtaining and documenting informed consent of the trial’s study participants.

**Investigational Device Exemption (IDE):** The means through which the sponsor technically obtains an exemption from the FDA to transport or distribute an unapproved device across state lines. The IDE allows the device to be used in a clinical trial to collect safety and efficacy/effectiveness data.
**Investigational New Drug (IND):** The means through which the sponsor technically obtains an exemption from the FDA to transport or distribute a new drug or biologic that is used in a clinical investigation across state lines. The IND allows the drug or biologic to be used in a clinical trial to collect safety and efficacy/effectiveness data.

**Investigator:** A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the “principal investigator” or the “site investigator”. A trial can have one investigator (PI) and/or multiple investigators (Co-Investigators).

**Investigator's Brochure:** A document that describes the study drug, its formulation and side effects.

**Key Personnel:** The PI and other individuals who contribute to the scientific development or execution of a clinical trial in a substantive, measurable way, whether or not they receive salaries or compensation under the contract.

**Medicare Contractors:** Companies hired by the government to oversee medical claims under the Medicare health insurance program.

**Monitoring Visits:** Site visits from sponsor or CRO personnel to oversee the progress of a clinical trial, and ensure that it is conducted, recorded, and reports in accordance with the protocol, standard operating procedures, GCP to the extent consistent with FDA and DHHS regulations and guidelines, and other applicable regulatory requirement(s).

**Multicenter Trial:** A clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator.

**Patient Care Costs:** Items, and services related to patient care that are rendered during a clinical trial (i.e., medical visits, hospital stays, lab tests, x-rays, etc.).

**Placebo:** A pharmaceutical preparation that contains no active agent. In blinded studies, the placebo is generally made to look just like the study drug.

**Preclinical Studies:** Animal studies that support Phase I safety and tolerance studies that must comply with GLP. Data about a drug’s activities and effects in animals help establish boundaries for safe use of the drug in subsequent human testing (clinical trials). Because many animals have much shorter life spans than humans, preclinical studies can provide valuable information about a drug’s possible toxic effects over an animal’s life cycle and on its offspring.
**Prime Recipient (Prime Site):** An individual or organization performing a clinical trial that has contracted with another individual or organization to be a site for a clinical trial under the terms of its contract with the sponsor.

**Principal Investigator (PI):** See Investigator definition

**Prospective Reimbursement Analysis (PRA or Coverage Analysis):** A systematic review of a clinical research study protocol and other related documents to determine and record with costs are billable to a participant or third party and which costs must be paid for by the sponsor or research account. The PRA consists of a memo format of study information that can be used to create a billing grid for items or services.

**Protocol:** A study plan on which a clinical trial is based. The plan is carefully designed to safeguard the health of the participants as well as to answer specific research questions. A protocol describes what types of people may participate in the trial; the schedule of tests, procedures, medications, dosages; and the length of the study.

**Protocol Amendment:** A written description of a change(s) to, or formal clarification of, a study plan.

**Randomization:** The distinguishing features of a clinical trial whereby, after the assessment of eligibility and recruitment, but before the intervention begins, study participants are randomly allocated to receive one or another treatment under the study. After randomization the two (or more) groups are monitored in exactly the same way. The only difference is in the care or administration of the drug or device that the members of each group receive. (Assigned by chance, like flipping a coin.)

**Research Patient Care Rate Agreement:** Agreement negotiated between a hospital and the DHHS. The rates in the agreement must be used in all requests and/or claims for reimbursement of research patient care costs from a federal agency under a federally sponsored clinical study and are based upon a hospital’s Medicare Cost Report which is submitted annually to DHHS.

**Schedule of Events (SOE):** A compilation of the activities that take place with the study participant during screening and at each scheduled visit according to the protocol.

**Screen Failures:** Potential study participants who are not selected to participate in a clinical trial because they do not meet the criteria outlined in the protocol.

**Serious Adverse Event (SAE):** Any untoward medical occurrence that at any dose: results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; or results in a congenital anomaly/birth defect.
**Sponsor:** An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial. According to 21 CFR 50.3, a corporation or agency whose employees conduct the investigation is considered a sponsor and the employees are considered investigators.

**Sponsor-Investigator:** An individual who both initiates and conducts (alone or with others) a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a study participant. The term does not include any person other than an individual (e.g., it does not include a corporation or an agency). The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.

**Standard of Care:** A treatment regimen or medical management plan based on state of the art patient care for a particular disease or condition.

**Standard Operating Procedures (SOP):** A step-by-step procedure that promotes uniformity in operations to help clarify and augment such operations. SOP’s document the way activities are to be performed to facilitate consistent conformance to technical and quality system requirements and to support data quality.

**Study Closeout:** Initiated by the PI and/or study team when a clinical trial is completed and no further study related revenues or expenses are expected. It is the process by which the various accounts associated with a clinical trial are closed.

**Study site:** Location(s) where the study will be conducted. See also Subcontractors definition.

**Subcontractor:** An individual or organization under contract with a prime recipient to perform a clinical trial. Clinical trial subrecipients are referred to as study sites.

**Subrecipient:** An investigator/site functioning or receiving funding and/or services under the prime agreement.

**Unrelated Business Income Tax (UBIT):** A tax that is assessed on not-for-profit organizations for activities that are unrelated to their charitable, tax-exempt status (e.g., for universities or academic medical centers, this may include bookstores, dining services, or leased space).
Grant/Clinical Trial Checklist

PRF#: _______________   CON#: _______________   Project#: _______________

PI: ____________________
CoPI: ____________________
Dept: ____________________
Notified Date: ________________

Primary Site (circle one): Y / N
Subaward (circle one): Y / N
Sponsor: ____________________
Dates: ____________________
F&A Rate: ____________________
Direct $: ____________________
F&A $: ____________________
Total $: ____________________

**Grants:**

☐ Do you have copies of the budget?
☐ Are there subawards to be issued?
☐ Is there equipment to purchase?
☐ Is there cost share?  ☐ IDC Sharing?
☐ Are there restrictions for:
  ☐ PI/Faculty Salary
  ☐ Travel- Domestic/Foreign
  ☐ Do Funds Revert: Y / N
  ☐ Rebudget Restrictions?
☐ Other (please list):

**Clinical Trial:**

TASCS#: ________________   On-Core#: ________________

# of Patients to Enroll:

1. Startup Funds? Y / N  Amount: $______________  Refundable: Y / N
2. Type of Award:  ☐ Cost Reimbursable  ☐ Fixed Fee  ☐ Mix
3. Do you have a copy of the:  ☐ Protocol  ☐ Payment Schedule
4. How is the revenue earned:  ☐ CRF’s  ☐ Milestones  ☐ Both
5. List billable expenses: ________________________________
6. Is there to be a hold back? Y / N  If yes, ____%
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<td>Coordinator Mtg</td>
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<td>y / n</td>
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<tr>
<td>7</td>
<td>Payroll Needed</td>
<td>y / n</td>
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<td>8</td>
<td>Changes To</td>
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**Tools for this information**

UMReports  
TASCS  
ON Core  
NOGA  
Study Budget
A Word about the 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. As most clinical trials are fixed price agreements, the investigator is obligated to perform the work described in the contract, even if the actual costs exceed the total contracted amount. 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.

A Word about the 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 both 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, MRI scans, etc. will be analyzed in the lab or at the sponsor’s site
- Determine if there will be professional charge required for the technical test performed. An example would be ECG w/interpretation by Cardiologist.
- Either edit the sponsor’s budget or create a spreadsheet to reflect all costs of the trial
- Negotiate a cost per patient to complete a clinical trial, not a cost per test or procedure
- It is permissible to use standard of care test results for clinical research
- It is not permissible to bill insurance for a test, device or service paid by the sponsor
- For multi-year trial, consider adding an inflation rate to the 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.

After discussing the above list of issues, it’s 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 for the personnel involved, the supplies, the testing to be done, and other costs of the work plus the Facilities & Administrative (F &A) cost. Divide the total estimated cost by the anticipated number of patients. In addition it is common to include start- up costs to be incurred regardless of the number of patients. For example, IRB fees are charged to the study but not calculated as part of the per patient costs.

Review Budget Template
Budget considerations:

Clinical Activities

Complete pricing (research rate) request in On-Core for the procedures using Fairview;

- Each clinical procedure
- Standard of Care vs clinical trial costs
- Outpatient clinic room
- Laboratory fees
- Central lab
- Pharmacy charges
- In patient room
- Radiology
- Operating rooms
- Anesthesia cost
- Other costs dependent on protocol

Personnel

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 week or month period.

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

Define amounts and time for:

- Per visit stipends
- Travel
- Meals
- Parking
- Recruiting

One Time Costs

- IRB Review Fees
- IRB Continuuing Fess
- IRB Amendment Review
- IRB Preparation Fee
- Investigational Drug Pharmacy set-up fee and storage or dispensing fees
- Archive document storage fee $rate/ year
- Source document binders per patient
- Publication costs
Administrative Costs

Obtain rates and/or amounts for:

- Facility & Administrative (F&A) costs. Most Universities classify their clinical trials for F & A purposes as “off-campus research”, which for federal sponsors is capped at 26%.
- Cancellation fee if sponsor terminates study. This provides the institution with some recovery of start-up costs and running the trial.

It is not unusual to negotiate with sponsors who may resist paying the institutionally approved F & A. Treat the rate as non-negotiable.

Less Common Expenses

The following list is a list of less common expenses, but 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 Forms (and translation costs for the benefit of subject whom English is not their first language)

Protocol Requirements

Translate the activity into a measure of time. How long does it take to complete set of vitals, as an example, how much time does a difficult blood draw take, packaging specimen for shipping, what about telephone follow up time? Also consider the following:

- Recruiting
- Explaining administration of a drug
- Screening
- Reviewing 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
- Maintaining the files
- 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 the study costs are included. Since it is usually necessary to negotiate aspects of the budget, the investigator should view the initial budget as a draft, revising 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.

Occasionally, initial payments will not be sent until a subject is randomized. This is not ideal. 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 non-refundable initial payment that will cover startup cost. This amount needs to be adequate to cover the costs incurred with initiating the trial including the IRB fees.

Look carefully at the milestone payments. Will payment be made upon completion of the CRFs? That may mean waiting until the monitor has reviewed the CRF’s and passed them on to data management. Will payment be on completion of a subject completion of the trial? 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 too large a deficit.

Sponsors also try to hold back a significant portion of the payment until all study activities are complete, 10% of the total budget is preferred, pay close attention, to this payment term because it can mean an unreasonable amount of time.

EXAMPLE – COMMON PAYMENT SCHEDULE
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
- Invoice permitted for other cost (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 Failure 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 I have tried to capture a significant portion.

**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 to two options when presenting a budget. Sponsors may offer a certain amount per patient and ask the investigator work within that amount or 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, F & A costs are not waived for industry sponsors. To do so would force the institution to subsidize the performance of industry sponsored research with institutional dollars, a generally undesirable situation.
<table>
<thead>
<tr>
<th>STUDY PROCEDURES / EVALUATIONS</th>
<th>Cost Per Unit</th>
<th>Pre-Transplant Screen/Baseline (1-2 Days Prior to Transplant)</th>
<th>Day 0 (Transplant, Pre-dose)</th>
<th>Day 1 (Post-dose)</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 7</th>
<th>Day 30</th>
<th>Day 90</th>
<th>Day 180</th>
<th>Day 365 Post-study Follow-up Telephone Contact</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical history</td>
<td>$ 100.00</td>
<td>$ -</td>
<td>$ -</td>
<td>$ -</td>
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</tr>
<tr>
<td>Physical examination</td>
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<tr>
<td>Vital signs</td>
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<td>$ -</td>
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<tr>
<td>EKG</td>
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<tr>
<td>Pt incentive for visit travel and parking for research visits per hour</td>
<td>$ 75.00</td>
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<td>$ -</td>
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</tr>
<tr>
<td>Room charge for visit(whole-day)</td>
<td>$ 100.00</td>
<td>$ -</td>
<td>$ -</td>
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<tr>
<td>Room charge for visit(whole-day)</td>
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<td>Clinical labs shipping</td>
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<tr>
<td>Serum creatinine</td>
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<td>$ -</td>
<td>$ -</td>
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<td>Record Total Urine Volume</td>
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<tr>
<td>Twenty-four hour timed urine collection for creatinine clearance</td>
<td>$ 50.00</td>
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<tr>
<td>Urine creatinine</td>
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<tr>
<td>Pharmacy dispensing fee</td>
<td>$ 50.00</td>
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<td>PI fee</td>
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</tr>
<tr>
<td>Institutional Overhead</td>
<td>26%</td>
<td>$ -</td>
<td>$ -</td>
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<td>$ -</td>
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<tr>
<td>Total Direct Cost</td>
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</tr>
<tr>
<td>Institutional Start-up Costs</td>
<td>$ 2,500.00</td>
<td>$ 650.00</td>
<td>$ 3,150.00</td>
<td>$ 3,150.00</td>
<td>$ -</td>
<td>$ -</td>
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<td>$ -</td>
</tr>
<tr>
<td>IRB application-related one time fee (IRB)</td>
<td>$ 2,182.54</td>
<td>$ 567.46</td>
<td>$ 2,750.00</td>
<td>$ 2,750.00</td>
<td>$ -</td>
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</tr>
<tr>
<td>Study set-up administrative fees (constructing transplant staff on study protocol and intervention, CRF, pt documents, set up Fairview research billing account in TANS, SPA contract negotiation, etc; one time fee)</td>
<td>$ 6,000.00</td>
<td>$ 1,560.00</td>
<td>$ 7,560.00</td>
<td>$ 7,560.00</td>
<td>$ -</td>
<td>$ -</td>
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<td>$ -</td>
</tr>
<tr>
<td>Pharmacy Start-up Fee</td>
<td>$ 1,817.46</td>
<td>$ 472.54</td>
<td>$ 2,290.00</td>
<td>$ 2,290.00</td>
<td>$ -</td>
<td>$ -</td>
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</tr>
<tr>
<td>Total Start Up</td>
<td>$ 12,500.00</td>
<td>$ 3,250.00</td>
<td>$ 15,750.00</td>
<td>$ -</td>
<td>$ -</td>
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</tr>
</tbody>
</table>

**Start-up Costs**

<table>
<thead>
<tr>
<th>Cost Per Unit</th>
<th>Institutional Overhead (26%)</th>
<th>Total</th>
<th>Sponsor Budget Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>$ -</td>
<td>$ -</td>
<td>$ -</td>
<td>$ -</td>
</tr>
</tbody>
</table>

**Cost Items per event**

- **Pregnancy test (in blood or urine) for women of childbearing potential**: $ 50.00
- **Revised Consent Charge(per subject)**: $ 80.16
- **DSD Safety Report (each)**: $ 25.00
- **Changes to probable Amendments/revision to IRB per event**: $ 150.00
- **Pathology services - Histologic review of clinically-indicated biopsy tissue (per the 2007 revisions to the Banff '97 classification)**: $ 400.00
- **FDA Audit Fee**: $ 2,500.00
- **Serious Adverse Event Reporting Fee (Per SAE)**: $ 500.00
- **Monitor Visit**: $ 500.00
- **Maintenance Fees (paid monthly for the duration of the study until 1st subject enrolled)**: $ 300.00

03June2010, v. 1.0
Regulatory maintenance fees will be charged at the time of each IRB continuing review approval. Regulatory maintenance includes submitting and obtaining 

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
<th>$15.87</th>
<th>$2,500.00</th>
<th>$2,500.00</th>
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<tbody>
<tr>
<td>End of Study Archival Fee</td>
<td>$793.85</td>
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<tr>
<td>Close out fees</td>
<td>$1,500.00</td>
<td>$100.00</td>
<td>$1,890.00</td>
<td>$1,890.00</td>
</tr>
</tbody>
</table>

**SUBTOTAL** $7,568.34 $1,067.77 $9,158.11 $9,158.11

**TOTAL** $20,068.34 $5,217.77 $24,908.11 $24,908.11

Date Budget Approved:

03June2010, v. 1.0
<table>
<thead>
<tr>
<th>Start-up Costs</th>
<th>Cost Per Unit</th>
<th>Institutional Overhead (26%)</th>
<th>Total</th>
<th>Sponsor Budget</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRB start-up fee - one time paid to IRB</td>
<td>$2,500.00</td>
<td>$650.00</td>
<td>$3,150.00</td>
<td>$ (3,150.00)</td>
<td></td>
</tr>
<tr>
<td>IRB application-initial one time fee (80hrs)</td>
<td>$2,182.54</td>
<td>$567.46</td>
<td>$2,750.00</td>
<td>$ (2,750.00)</td>
<td></td>
</tr>
<tr>
<td>Study set-up administrative fees (instructing transplant staff on study protocol and intervention, CRF, pt documents, set up Fairview research billing account in TASCS, SPA contract negotiation, etc; one time fee)</td>
<td>$6,000.00</td>
<td>$1,560.00</td>
<td>$7,560.00</td>
<td>$ (7,560.00)</td>
<td></td>
</tr>
<tr>
<td>Pharmacy Start up Fee</td>
<td>$1,817.46</td>
<td>$472.54</td>
<td>$2,290.00</td>
<td>$ (2,290.00)</td>
<td></td>
</tr>
<tr>
<td>Total Start Up</td>
<td>$12,500.00</td>
<td>$3,250.00</td>
<td>$15,750.00</td>
<td>$ -</td>
<td>$ (15,750.00)</td>
</tr>
<tr>
<td>Invoice item(some one time; some per event)</td>
<td>Cost 1</td>
<td>Cost 2</td>
<td>Cost 3</td>
<td>Cost 4</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>Pregnancy test (in blood or urine) for women of childbearing potential</td>
<td>$ 50.00</td>
<td>$ 13.00</td>
<td>$ 63.00</td>
<td>$ (63.00)</td>
<td></td>
</tr>
<tr>
<td>Revised Consent Charge(per subject) This fee is to support PI and Coordinator time, as well as administrative costs incurred for re-consenting a subject. This cost is payable upon receipt of an invoice from the Institution.</td>
<td>$ 80.16</td>
<td>$ 20.84</td>
<td>$ 101.00</td>
<td>$ (101.00)</td>
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<tr>
<td>IND Safety Report (each)</td>
<td>$ 25.40</td>
<td>$ 6.60</td>
<td>$ 32.00</td>
<td>$ (32.00)</td>
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<tr>
<td>Changes to protocols/Amendments/revision to IB per event</td>
<td>$ 750.00</td>
<td>$ 195.00</td>
<td>$ 945.00</td>
<td>$ (945.00)</td>
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</tr>
<tr>
<td>Pathology services - histologic review of clinically-indicated biopsy tissue (per the 2007 revisions to the Banff '97 classification)</td>
<td>$ 400.00</td>
<td>$ 104.00</td>
<td>$ 504.00</td>
<td>$ (504.00)</td>
<td></td>
</tr>
<tr>
<td>FDA Audit Fee: This daily fee is to support PI and Coordinator time to be available for the FDA auditors to answer questions, provide documentation, and prepare correspondence as requested by the auditor. This cost is payable upon receipt of an invoice from the Institution.</td>
<td>$ 600.00</td>
<td>$ 156.00</td>
<td>$ 756.00</td>
<td>$ (756.00)</td>
<td></td>
</tr>
<tr>
<td>Serious Adverse Event Reporting Fee (Per SAE)This fee is for each local SAE (including follow-up), upon receipt of an invoice from the Institution. We will invoice for all SAE's. The cost of AE's is figured into the per-patient cost. (Assumes 4 hours CRC time, 1 hour of PI time)</td>
<td>$ 500.00</td>
<td>$ 130.00</td>
<td>$ 630.00</td>
<td>$ (630.00)</td>
<td></td>
</tr>
<tr>
<td>Monitor Visits This daily fee is to support PI and Coordinator salaries to be available for the study monitor to answer questions, provide documentation, and resolve queries, and costs associated with dedicated monitoring space. This cost is</td>
<td>$ 500.00</td>
<td>$ 130.00</td>
<td>$ 630.00</td>
<td>$ (630.00)</td>
<td></td>
</tr>
<tr>
<td>Pharmacy Maintenance Fee: Start 1 year after receiving study drug, billed monthly till IP is returned or destroyed. This will be billed per quarter.</td>
<td>$ 85.00</td>
<td>$ 22.10</td>
<td>$ 107.10</td>
<td>$ (107.10)</td>
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<tr>
<td>Maintenance Fees (paid monthly for the duration of the study until 1st subject enrolled)</td>
<td>$ 300.00</td>
<td>$ 78.00</td>
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</tr>
<tr>
<td>Regulatory maintenance fees will be charged at the time of each IRB continuing review approval. Regulatory maintenance includes submitting and obtaining IRB</td>
<td>$ 1,984.13</td>
<td>$ 515.87</td>
<td>$ 2,500.00</td>
<td>$ (2,500.00)</td>
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<tr>
<td>End of Study Archival Fee</td>
<td>$ 793.65</td>
<td>$ 206.35</td>
<td>$ 1,000.00</td>
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<tr>
<td>Close out fees</td>
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<td>$ 390.00</td>
<td>$ 1,890.00</td>
<td>$ (1,890.00)</td>
<td></td>
</tr>
</tbody>
</table>
| **SUBTOTAL**                                                                                             | $ 7,568.34 | $ 1,967.77 | $ 9,158.11 | $ (9,158.11)**