HOW TO CONDUCT CLINICAL TRIALS SUCCESSFULLY AT UAB

PROCEDURE MANUAL
Department of Neurology
University of Alabama at Birmingham

OCTOBER, 2003
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PART I: STEPS FOR PREPARING, ASSESSING, INITIATING, FINANCIALLY MANAGING AND CLOSING OUT CLINICAL TRIALS

I. STEPS INVOLVED IN PREPARING FOR A SUCCESSFUL CLINICAL TRIAL

A. Assessing the clinical and fiscal viability of a clinical trial
   1. Assess the scientific and potential therapeutic importance of the study.
   2. Assess the suitability of the study for your program.
   3. Determine if you have access to patients that are suitable for the study.
   4. Determine if you have the expertise, time, support staff, space, and other logistical resources available to successfully execute the study.
   5. Assess if the timetable for patient recruitment and enrollment in the study is feasible and practical.
   6. Assess the proposed budget for fiscal viability, i.e., can you do the study for the Per Patient Budget proposed by the sponsor?
      a. You must have a line item budget to determine this.
      b. If the budget is inadequate; negotiate with the sponsor based on your costs for each of the activities/procedures in the proposed schedule of assessments.

B. Assessing a clinical trial budget
   1. Obtain schedule of assessments master grid from the study protocol.
   2. Fill in your direct cost of performing each activity and roll up your “per patient costs” for a completed patient.
   3. Calculate your indirect cost (at least 24%; best to negotiate higher (i.e. 29%) per patient.
   4. Combine direct costs and indirect costs per completed patient to obtain your total cost per completed patient.
   5. Compare your total cost per completed patient with what the sponsor has offered.
      a. If costs are positive, you are in good shape and the research project should be fiscally sound.
      b. If costs are negative, obtain and examine the sponsor’s line item budget and renegotiate item by item to obtain adequate funding to allow you to successfully complete the study.
(See Appendix A - How to determine financial feasibility of a clinical trial from a sponsors budget: Practical Tips)

C. Assessing the proposed payment schedule
   1. Start-up funds – to be used to open the grant account and to fund initial study related costs. This is usually an amount equal to the charge for 1 or 2 patients completing the study or a portion of the study.
   2. Frequency of monitoring visits and invoicing for activities/procedures performed versus quarterly payments
   3. Carefully consider the final payment/ “hold out” fee that is paid after all CRF’s are complete and all queries addressed (try to decrease to 10 – 15%).
   4. Require payment for large ticket/expensive procedures before actually done or invoice immediately with guarantee of rapid payment (e.g., surgery, PET scans, etc.).

D. Assessing “pass through” expenses:
   1. IRB package submission fee and renewal fees
      a. Direct to the IRB: $1500 (plus Indirect Costs of 25-30%: $375-450; total $1875-$1950).
      b. Your cost of preparing and submitting the package: $1000-$2500 (depending on the complexity of the study plus IDC 25-30%: $1250 - $3250)
   2. Cost of advertising
   3. Patient stipend/travel expenses
      *Remember to add in your indirect rate automatically for each of these expenses

E. Building an Internal UAB Budget
   1. University expenses (direct costs) must be reflected in the budget:
      a. Personnel (salary and fringe benefits)
      b. Office and clinical supplies
      c. Pharmacy fees
      d. Laboratory fees
      e. Patient reimbursement fee (e.g., travel, parking)
      f. Publication costs
      g. Institutional Review Board – Initial Review Fee: $1500
   2. The budget must total the estimated patient costs plus all one-time allowable fees.
   3. Industry sponsored clinical trials must use the indirect cost rate of 24% (or more if your department is to receive a portion for infrastructure support).
4. Examples of Internal Budgets
   a. Example of a well negotiated line item budget from the sponsor, followed by the UAB internal budget. This budget is fiscally sound because it covers salaries and procedures appropriately. It includes line items that reflect real, but “hidden” costs. These costs pertain to effort that can be expressed as follows: eligibility criteria; consent form; adverse events; investigator fee; and coordinator fee (in bold).

   **Budget A: Well Negotiated**

<table>
<thead>
<tr>
<th>Hypertension Study</th>
<th>Visit 1</th>
<th>Visit 2</th>
<th>Visit 3</th>
<th>Visit 4</th>
<th>Termination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Budget A: Sponsor’s Line Item Budget</td>
<td>Day 7</td>
<td>Day 30</td>
<td>Day 60</td>
<td>Day 90</td>
<td>Day 120</td>
</tr>
<tr>
<td>Eligibility Criteria</td>
<td>25</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Consent Form</td>
<td>200</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>History &amp; Physical</td>
<td>200</td>
<td>200</td>
<td>200</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>Vital Signs</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>ECG</td>
<td>200</td>
<td>200</td>
<td>200</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>Venipuncture</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Electrolyte Panel</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Adverse Events</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Investigator Fee</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Coordinator Fee</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Patient Stipend</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Subtotal</td>
<td>1000</td>
<td>275</td>
<td>275</td>
<td>275</td>
<td>375</td>
</tr>
<tr>
<td>Indirect Costs (24%)</td>
<td>240</td>
<td>66</td>
<td>66</td>
<td>66</td>
<td>90</td>
</tr>
<tr>
<td>Total by Visit</td>
<td>1240</td>
<td>341</td>
<td>341</td>
<td>341</td>
<td>465</td>
</tr>
</tbody>
</table>

Total per patient charge, including indirect cost = $3,069.00
For pass through budget:
   Advertising Costs = $1,300.00
   IRB Fee = $2,600.00

**Hypertension Study**

<table>
<thead>
<tr>
<th>Budget A: Internal Budget</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 Patients at $3069.00/pt. = $30,690.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1. Personnel</th>
<th>Salary</th>
<th>Fringe</th>
<th>Total</th>
<th>% Effort</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. PI</td>
<td>5,000</td>
<td>1,080</td>
<td>6,080</td>
<td>5% of 100K (Budget pays effort sufficiently)</td>
</tr>
<tr>
<td>b. RN</td>
<td>10,000</td>
<td>2,500</td>
<td>12,500</td>
<td>25% of 40K (Budget pays effort sufficiently)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>18,580</td>
<td></td>
</tr>
</tbody>
</table>

| 2. ECG's     |        |        | 2,000 |          |
| 3. Lab       |        |        | 1,000 |          |
| 4. Patient Travel |    |        | 1,500 |          |
| 5. Supplies, postage, photocopying |    |        | 170.00|          |
| 6. IRB Fee   |        |        | 1,500 |          |

Total Direct Costs = 24,750.00
Indirect Costs (24%) = 5,940.00
GRAND TOTAL = $30,690.00

Note: IRB Fee to be invoiced by the study site.
Advertising to be invoiced by the study site.
b. Example of a similar line item budget from the sponsor, but the budget was poorly negotiated. Following is the UAB internal budget. This budget is not fiscally sound. It is too low to cover salaries appropriately.

**Budget B: Poorly Negotiated**

<table>
<thead>
<tr>
<th>Hypertension Study</th>
<th>Budget B: Sponsor’s Line Item Budget</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>$1,302.00 per patient</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Visit</strong></td>
<td><strong>Screen</strong></td>
</tr>
<tr>
<td>History &amp; Physical</td>
<td>200</td>
</tr>
<tr>
<td>Vital Signs</td>
<td>50</td>
</tr>
<tr>
<td>ECG</td>
<td>200</td>
</tr>
<tr>
<td>Venipuncture</td>
<td>50</td>
</tr>
<tr>
<td>Electrolyte Panel</td>
<td>50</td>
</tr>
<tr>
<td>Patient Stipend</td>
<td>25</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td>575</td>
</tr>
<tr>
<td>Indirect Costs (24%)</td>
<td>138</td>
</tr>
<tr>
<td><strong>Total by Visit</strong></td>
<td>713</td>
</tr>
</tbody>
</table>

Total per patient charge, including indirect cost = $1302.00

For pass through budget:  
Advertising Costs = $1,300.00
IRB Fee = $2,600.00

---

<table>
<thead>
<tr>
<th>Hypertension Study</th>
<th>Budget B: Internal Budget</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>10 Patients at $1302.00/pt. = $13,020.00</strong></td>
<td></td>
</tr>
<tr>
<td><strong>1. Personnel</strong></td>
<td><strong>Salary</strong></td>
</tr>
<tr>
<td>a. PI</td>
<td>0</td>
</tr>
<tr>
<td>b. RN</td>
<td>3,200</td>
</tr>
<tr>
<td><strong>Total Salaries</strong> =</td>
<td>4,000.00</td>
</tr>
<tr>
<td>2. ECG’s</td>
<td>2,000.00</td>
</tr>
<tr>
<td>3. Lab</td>
<td>1,000.00</td>
</tr>
<tr>
<td>4. Patient Travel</td>
<td>1,500.00</td>
</tr>
<tr>
<td>5. Supplies, Postage, photocopying</td>
<td>500.00</td>
</tr>
<tr>
<td>6. IRB Fee</td>
<td>1,500.00</td>
</tr>
<tr>
<td><strong>Total Direct Costs</strong></td>
<td>10,500.00</td>
</tr>
<tr>
<td><strong>Total Indirect Costs (24%)</strong></td>
<td>2,520.00</td>
</tr>
<tr>
<td><strong>GRAND TOTAL</strong></td>
<td>13,020.00</td>
</tr>
</tbody>
</table>

The costs of the line item procedures in the schedule of assessments (lab, ECG, patient travel) are covered in Budget B. But other real, but “hidden” costs are not covered. These costs pertain to effort that is not represented in a procedure or assessment. You should negotiate for these “hidden” costs, adding them as a line in the Sponsor’s budget. Examples are: Eligibility criteria; consent form; adverse events; investigator fee; coordinator fee.
II. STEPS INVOLVED IN INITIATING A CLINICAL TRIAL
Two processes should take place in parallel: A. IRB Submission, and B. Contract (OGCA) Submission

A. Navigating the IRB Process – Submit the protocol oversight review form signed by a professor (i.e. Watts, Oh, King, Faught, Harrell or Rosenfeld), consent form (for research involving children and/or minors less than 19 years of age, one copy of a memorandum from the PI which must address as the Children’s Risk level assessment), Human Subjects Protocol (which includes any advertisements, newsletters, flyers, recruitment letters… and investigational drug brochure), a copy of the completed 1572 form, approval from The Kirklin Clinic, University Hospital, The Children’s Hospital of Alabama and/or Callahan Eye Foundation Hospital, Sponsor Billing Form, if applicable, Waiver of Compliance Billing Language, if applicable and on copy, if applicable, of the sponsor’s protocol and/or the Funding Application(grant, letter requesting funding, etc.). If there is no outside funding source, address in a cover memorandum how the study costs will be paid.

1. Protocol Submission for Expedited Review: Expedited Review is applicable for research activities which involve no more than minimal risk to the human participants and which can be placed in one or more of the nine (9) categories listed on the application form (see section 10 of IRB guidebook) Categories one (1) through seven (7) pertain to both initial and continuing review. The definition of minimal risk for the purpose of IRB application is defined as the amount of risk encountered in daily life.

The expedited review procedure may not be used where identification of participants and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that the risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

The expedited review procedure may not be used for classified research involving human participants or for research involving human
participants or for research including any of the vulnerable population listed in item 6 of the Expedited Human Subject Protocol found in the section.

a. Application Requirements: Original Expedited Review application with a check by the category or categories which he/she is claiming for Expedited Review; Original Expedited Human Subjects Protocol.

b. Additional application requirements:
   i. Funding application and UAB Office of Grants and Contracts Administration (OGCA) Tracking #, if the study is externally funded.
   ii. Consent Form if, applicable
   iii. Any questionnaire, survey, and/or scripts to be used with participants.
   iv. Any materials to be used to recruit participants
   v. Specimen release form or approval letter if you are obtaining pathological or diagnostic specimens. The Chairman of the Department responsible for providing the specimens should sign the approval letter. If specimens are being obtained from Pathology, you should submit a signed copy of the Release of Pathologic Materials form.
   vi. Drug release form from the appropriate pharmacy (UAB or Children’s Hospital) for any drugs to be used in the protocol. The UAB Pharmacy Department can be reached at 934-2162 or the Children’s Hospital Pharmacy at 939-9718 for further information.
   vii. Faculty Advisor/Course Instructor’s name, signature and email address should be included on page three of the application if the Principal Investigator is a student.
   vii. If the research involves children it must comply with the Children’s Risk Level (CRL)#1 (45 CFR 46.404) – Research not involving greater than minimal risk. Minimal risk means that the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations of tests. Research in this category requires both assent of the child and permission of at least one parent or guardian.

c. Submission: The original Expedited Review application must be submitted. All materials should be mailed or delivered to Room 470, Administration Building (AB), Zip 0111. There are no deadlines for submission of expedited review applications. The
expedited review process takes approximately 3 weeks. If there are any questions, please call the IRB office at 934-3789.

d. Expedited Review for Research Involving Children: Expedited review is now allowed for research where children are the participants, except as noted.

e. IRB Approval: IRB approval is for one year, unless otherwise specified, commencing with the approval date. Research activities may not continue past the one-year anniversary date of the IRB approval date. The Investigator’s Progress Report form should be submitted no less than 4 weeks, preferably 8 weeks, prior to the end of the approval.

f. Final Report Instructions: If the project is completed, submit one copy of a final progress report. Use the Investigator’s Progress Report Form and check the “final report” box on the top of the form.

Findings from the study must be reported at this time if they have not already been reported to the IRB.

The IRB expects findings to be included for all studies that have been ongoing for five or more years.

2. Protocol Submission for IRB Full Review:

a. Human Subjects Protection (HSP): The IRB Human Subjects Protocol as shown enables the Investigator to furnish considerable background information with a minimum effort. Since a single protocol is used for all types of research some questions may not be applicable to the proposed study. Where questions may not apply enter “NA” in the space provided.

The Board requires that the forms provided in this guidebook be used for submitting protocols for review. The IRB insists that responses to the questions be clearly distinguished in a different font, type size or via some other means. Also, the pages should be in the same format as those provided in the guidebook.

The Investigator must complete the entire protocol including the outlined sections shown as items 11-15. Grant applications and/or sponsor’s protocols will not be accepted in lieu of answering the questions outlined in the instructions. Since many members of the IRB are by law nonprofessional, and even the professional members have technical expertise in limited areas, the use of understandable non-technical language is essential.
b. Protocol Submission Types
   i) Phase I/II Studies – Do not submit Phase I/II studies together. Submit the Phase I study and then, once the data from it has been evaluated, submit the Phase II portion as a separate study (unless there is a strong and justifiable objection from the sponsor). Data from the Phase I study should be evaluated before proceeding to the next phase.
   ii) Extension/Open-Label Phase IV Studies – These studies should be submitted as new studies. It is IRB policy to assign them a new IRB number and treat them as a separate study. Results from the previous study should be made available to the IRB and any adverse events should be incorporated into the open-label phase.
   iii) Study Tools – Copies of non-standardized quality of life or other questionnaires, diaries, etc. should be submitted with the protocol for review by the IRB.

c. Protocol Oversight Review Form – After your have your human subject protocol form and consent form completed please send these along with protocol oversight reviews form to one of the following physicians for review and approval: Dr. Ray Watts, Dr. Shin Oh, Dr. Peter King, Dr. R. Edward Faught, Dr. Lindy Harrell and Dr. Steven Rosenfeld

d. Submission Packet
   i) One complete set of the following documents should be sent to the IRB. This packet includes:
      a) Completed and signed IRB Human Subjects Protocol
      b) Completed and signed Protocol Oversight Review Form
      c) One copy of the consent form
      d) For research involving children and/or minors less than 19 years of age, one copy of a memorandum from the Principal Investigator which must address the Children’s Risk Level Assessment
      e) Release of Drugs for Human Research Use Pharmacy form(required for drug studies being conducted at UAB, TKC and Children’s Hospital)
      f) Radiation safety approval, if applicable
      g) Release of Pathologic Materials form, if applicable
      h) Infection Control Memorandum, if applicable
      i) Approval from TKC, University Hospital, The Children’s Hospital of Alabama and/or Callahan Eye Foundation
      j) Documentation/verification of the sponsor’s injury compensation policy
k) Sponsor Billing Form, if applicable
l) Waiver of Compliance Billing Language, if applicable
m) One copy, if applicable, of the sponsor’s protocol and/or the Funding application (grant, letter requesting funding, etc.). If there is no memorandum how the study cost will be paid.
n) One copy of the Investigator’s Brochure for studies using an investigational new drug or the package insert for studies using commercially available drugs in an investigational manner and one copy of the FDA 1572 form.

2. Other Site Approvals Required
a. Research conducted at the Jefferson County Department of Health:
   A special review panel, which includes employees of the Health Department, as well as a faculty member (previously identified) from the Department must review all studies conducted at the Health Department.

b. Research Conducted at the Veterans Administration Medical Center (VAMC): UAB and the Birmingham Veterans Administration Medical Center (BVAMC) have a cooperative amendment on file with the Office for Human Research Protections. The amendment allows UAB faculty to rely on the review by the VA IRB for research that meets all of the following requirements:
   - the UAB researcher must have a joint appointment with the VA;
   - participants are accrued exclusively at the VA;
   - the research is conducted using funds provided through the VA or its non-profit organization (VISTAR).

UAB faculty relying on the VA IRB will still need to submit the following document to the UAB IRB for administrative review.
   ✓ One copy of the protocol submitted for VA IRB review
   ✓ Once copy of the VA IRB approval form
   ✓ One copy of the VA IRB approved consent form

At the time of regular protocol renewal, UAB faculty relying on the VA IRB will need to submit the following documents for UAB IRB review.

   ✓ One copy of the protocol renewal materials submitted to VA IRB review
   ✓ One copy of the VA IRB approval form
   ✓ One copy of the VA IRB approved consent form
The UAB IRB may in rare situation require review by a UAB IRB as well. However, this will not affect the BVAMC review. Any time human subjects will be seen at both institutions, usually both IRBs will provide review. Investigators may contact Ms. Barbara Price at ACOS for Research and Development, VA extension 12-6430 for more information regarding the VA IRB and application materials.

c. Research Conducted at The Children’s Hospital of Alabama (TCHA): All research conducted at TCHA involving dispensing of drugs to human participants must be registered with the TCHA Pharmacy Department. Investigators should contact the Pharmacy Department at 939-9718 for information and application materials.

For studies being conducted utilizing The Children’s Hospital of Alabama, investigators need to notify Christi Napper in Administration with the following information: PI, Study Title, Study Coordinator, Department and Sponsor for the study. This can be done by email to Christi.napper@chsys.org prior to submitting the application to the IRB. Administration will respond back by email confirming the notification. This email confirmation notice (one copy only) should be included with your original Human Subjects Protocol application to the IRB at the time of submission.

d. Research Conducted at The Kirklin Clinic (TKC): For studies being conducted utilizing TKC investigators need to notify Penny Phillips, RN with the following information: PI, Study Title, Study Coordinator, Department and Sponsor of the study. This can be done by email to pphilips@uabmc.edu or by telephone (801-8707) prior to submitting the application to the IRB. Clinical Support Services will respond back by email confirming the notification. This email confirmation notice (one copy only) should be included with your original Human Subjects Protocol application to the IRB at the time of submission.

e. Callahan Eye Foundation Hospital (EFH): For studies being conducted utilizing EFH investigators need to notify Leigh Aufdemorte with the following information: PI, Study Title, Study Coordinator, Department and Sponsor of the study. This can be done by email to laufdemorte@uabmc.edu prior to submitting the application to the IRB. She will respond back by email confirming the notification. This email confirmation notice (one copy only) should be included with your original Human Subjects Protocol application to the IRB at the time of the submission.
f. University Hospital (UH): For studies being conducted utilizing UH, investigators need to notify Elvora (Ivy) Cook, Manager Patient Financial Services (PFS) with the following information: PI, Study Title, Study Coordinator, Department and Sponsor of the study. This can be done by email to (icoo@uabmc.edu) or by telephone (975-6938) prior to submitting the application to the IRB. PFS will respond back by email confirming the notification. This email confirmation of notice (one copy only) should be included with your original Human Subjects Protocol application at the time of submission.

3. Vulnerable Subject Populations
   a. Federal regulations require more rigorous protection of human subject populations that are considered especially vulnerable.
      i) Cognitively impaired subjects:
      ii) Female subjects of child-bearing potential. The issue of pregnancy prevention and concerns should be addressed in the main body of the consent.
      iii) Prisoners or incarcerated subjects

4. UAB’s Assent Policy: Assent means the potential participant’s affirmative agreement to participate in the research. Mere failure to object should not, in the absence of affirmative agreement, be construed as assent. The following list indicates how assent of children should be handled for children of different ages.
   a. For children less than 7 years of age, the child is assumed to be incapable of giving assent (see “Parental Consent” below).
   b. For children ages 7 years old to age 19, the parent or legal guardian must sign the consent form in addition to obtaining the assent of the child/minor or documentation of the reason for waiver of the assent is required. Assent of the child/minor may be waived if the capability of the child to give assent is judged limited by age, maturity or psychological state.
   c. The IRB will review, on a case by case basis, studies in which adolescents (14-19 years of age or ≥ 12 years of age in the case of STDs) will be participating and in which the investigator requests an exception to parental consent. The IRB will base its decision on applicable state law.

Parental Consent:
- If the proposed research involves no more than minimal risk, or is of possible direct benefit to the child, the consent of one parent is required.
- If the research involves greater than minimal risk without direct individual benefit, permission must be
obtained from both parents unless there is only one reasonably available parent. Guardian consent should be substituted for parental under appropriate legal constraints.

➢ The Investigator may request a waiver of parental or guardian consent if the research design does not require such consent to protect the participants (for example, neglected or abused children), provided an appropriate protection mechanism is substituted.

➢ Special provisions must be made for children who are wards of the state of any other agency, institution or entity to be included in research involving greater than minimal risk without direct individual benefit.

B. Submit the Clinical Trial Agreement (CTA; “Contract”) which contains the legal contractual agreement between UAB and the Sponsor, the Per Patient Budget, and the Payment Schedule to the Office of Grants and Contracts Administration (OCGA) for review, negotiation (if needed), and approval. (Should take 2-4 weeks). (Remember to submit the OCGA package and the IRB package in parallel.)

1. Investigator-initiated INDs
   a. IND – Investigational New Drug application (FDA 1571)
   b. Guided by Federal Regulation: 21CFR 312
   c. Investigator assumes responsibilities of the sponsor

2. Investigator-initiated Clinical Trials
   a. IND is required when an investigational compound is used in humans
   b. IRB defines when an IND is required
   c. Can have complicated contractual issues to sort out
      i) Indemnity and liability protection
      ii) Invention rights and ownership
      iii) Conflicts of Interest

3. Important Contract Issues for Clinical Research
   a. “Standard” clinical trial contract – 12-15 sections and about 10-12 pages of language
   b. Most important sections are: confidentiality, publication, intellectual property, indemnification, and budget/payment schedule
   c. Others are: termination, regulatory compliance, and data ownership
d. Confidentiality – “everything we give you and everything you do for the study”, length of time, patient confidentiality, exceptions
e. Publication – right to publish independently and without restrictions, “approval” vs. “review”, non-profit status

4. Common Challenges in Executing Contracts
   a. Incomplete information upon submission
   b. CRO as “go-between” for sponsor
   c. Waiting for response/poor communication
   d. Un-constructive negotiation (“no” vs. alternatives)
   e. Waiting for compliance approvals, originals for signatures
   f. Transport of documents and getting signatures

Once the protocol has IRB approval and the Contract has been executed, a study grant number will be assigned by the Office of Grants & Contracts Accounting (OGCA) via a fully executed contract. After receiving a grant account number:

C. Allocate study personnel and your percent effort to the clinical trial research grant account when an account number is assigned and the study begins.

D. Create and submit a Clinical Trials Billing Notification
   1. What is a clinical trials billing notification? Participants in a clinical trial or clinical research may be provided services by part of the UAB Health System, i.e. UAB Hospital, The Kirklin Clinic, Eye Foundation Hospital, etc. To meet federal and state regulatory compliance guidelines, a Clinical Trial Billing Process has been developed to identify both inpatients and outpatients who are enrolled in a clinical study.

   2. Registration of The Trial: At approval or termination of a trial, the top section of the clinical trial billing notice should be completed in full and faxed to the central fax number on the bottom of the form. This provides information to the billing entities about ongoing trials and the appropriate billing contacts for each trial. All trials, for which there is a potential for UAB Health System entities, i.e., Hospital, labs, Kirklin Clinic, etc., to render billable clinical services to research participants, should be registered.

   3. Patient and Visit Specific Information: The completed top section of the form should be duplicated as needed, and the remaining information completed for each protocol driven visit. Once again, the form should be faxed to the central fax number at the bottom of the form. This process provides patient and visit specific communication to the billing offices so that claim may be submitted appropriately to either the study or to insurance.

   4. Requesting Radiology/Laboratory Services as Part of a Clinical Trial: When requesting/ordering radiology/lab services performed as part of
a research protocol, the requestor should indicate the name of the study at order entry. The name of the study can be entered into the free text field in the PIN system, or shared with the scheduling clerk when ordered verbally. Radiology Technologists need this information before performing the test to ensure that the service is provided according to the protocol.

5. The Clinical Trial Billing notice should be completed by the Principal Investigator/Nurse Coordinator at the time of service indicating whether the radiology service is billable to the study or to the patient’s insurance.

G. Develop a Recruitment Plan. The goal of the UAB Health Systems Marketing Office is to assist you in locating patients with specific inclusion/exclusion criteria.

1. This includes several steps:
   a. Posting your study on the UAB Health System’s website, as well as the UAB Intranet, Medical Staff website, and the Editor’s group website. In addition, this office will assist in having the study published in the UAB Synopsis. For more information please contact Dr. Lynn at 934-2283 or the UAB Health System’s website at www.health.uab.edu/insight.
   b. Posting your study with HealthFinders. The purpose of HealthFinders is to prescreen patients who are interested in enrolling in a study. The patient calls the HealthFinders telephone number and is screened by a live nurse who knows the criteria for the study. For information please contact Daphne Hoyt at 934-6890 or dhoyt@uabmc.edu

2. Advantages of Involving the UAB Health System’s Marketing Office
   a. Listing the study with Health System’s increases awareness of the study
   b. Researchers have access to data indicating the success of media related to their study
   c. Trained nurses can prescreen callers interested in being a part of research studies and provide information to researchers conducting the study
   d. Increased patient satisfaction by speaking to a live person during the initial inquiry
   e. Ineligible participants are screened and identified, saving the clinical research coordinator time
3. Advertising/Recruitment Ideas
   a. Advertise on the UAB Health System’s Marketing website
      i) Goal is to have web listing of all active clinical trials that
         involve patient recruitment
      ii) Need IRB approved advertising copy for each clinical trial. If
         a specific drug name is advertised, sponsor approval must be
         obtained.
      iv) The IRB-approved form must be sent to the UAB Health System’s
         Marketing Office attention Dr. Lynn prior to being placed on
         the website.
   b. Direct mail: Utilize mailing lists to reach specific populations
   c. Print (Newspapers, magazines)
      i) Calendar listings for seminar on clinical issues
      ii) Send information and follow-up with phone call
   d. Radio
      i) Target station based on listenership
      ii) Call news staff
      iii) Call public service staff
   e. Newsletters
   f. Support groups
   g. Societies
   h. Advocacy groups
   i. Volunteer groups, etc.
   j. Churches/Synagogues
   k. Focus on advisory groups for your study
   l. Television - news story on the disease or procedure
   m. Community Outreach
   n. Health fairs

4. Recruit and enroll appropriate patients in a timely manner. Evaluate
   Recruitment Plan periodically and amend as needed.

III. STEPS INVOLVED IN EXECUTING A CLINICAL TRIAL
   A. Complete all study visits according to the protocol on enrolled patients.
   B. Submit required documentation to the IRB, including adverse events,
      renewals, protocol amendments, change in study personnel, etc.

IV. STEPS INVOLVED IN FINANCIALLY MANAGING A CLINICAL TRIAL
   A. Assess the number of patient visits and procedures conducted. Determine if
      payments are being made on schedule to make sure the account is funded in
      a timely manner. Usually the sponsor invoices itself based on the Clinical
      Research Associate’s periodic monitoring visits.
B. Reconcile assessments performed and related expenses with payments made by the sponsor utilizing the Financial Accounting System (FAS). Invoice the sponsor for uncollected revenue.
C. Once the contract is executed, Office of Grants and Contracts Accounting is the primary point of contact for payments, financial management, accounting transactions and internal systems.

V. STEPS INVOLVED IN CLOSING OUT A CLINICAL TRIAL

A. Contract should either be closed or officially extended within 90-120 days of the budget termination date.
   Approximately 75 days before the termination date, a letter will be issued reminding the PI to either prepare to close out the award or to request an extension for the account.
B. Complete all parts of the Case Report Forms (CRF) for each patient enrolled (i.e. answer all queries from the Sponsor).
C. Remove study personnel salaries from the clinical trial research grant account at the appropriate time.
D. Make sure that all payments have been received from the sponsor including the final “hold-out” payment. (Be sure all “pass through” expenses have been invoiced and received.)
E. Account for residual amount with Office of Grants and Contracts Accounting and your department. If appropriate, transfer residual to PI’s residual/recharge account.
   1. Return advances or unearned payments to sponsor
   2. Fund/clear overruns
   3. Freeze and delete account from the accounting system
   4. Maintain historical accounting records
   5. Audit liaison
G. Terminate the study with the IRB by submitting a termination form.
H. Remember that you must store all study-related source documentation according to FDA guidelines and the sponsor’s contract. (How will you pay for this?)
VI. CRITICAL SUCCESS FACTORS THAT MAKE AN ACADEMIC HEALTH CENTER ATTRACTIVE TO PHARMACEUTICAL AND BIOTECHNOLOGY COMPANIES

A. Superior expertise of the research team (Investigator(s), Nurse Coordinator, Regulatory/Administrative Staff)
B. Accessibility of large, well characterized patient base
C. Reputation of the Institution as a leading center for clinical care and research
D. Supportive clinical research environment
E. Timely completion of IRB approval, contract and budget negotiation, and processing of regulatory documents
F. Rapid enrollment of well-suited patients and successful completion of the study
G. “Track record” of excellent performance for the Investigator and Institution

*Success begets success!
PART II: ADDITIONAL RESOURCES, DEPARTMENTS AND INFORMATION PERTAINING TO RESEARCH AT UAB

I. INDIRECT COSTS
   A. Indirect costs are REAL expenditures associated with the university’s research activities. Unlike direct costs, IDC cannot be linked directly with a specific project
   B. The Indirect Costs (IDC) of Research Activities
      1. Facilities upkeep & renovation of buildings; heating/cooling; facilities and equipment interest and depreciation
      2. Administration -- accounting; general admin.; sponsored projects admin.; departmental admin.; libraries
      3. Federal and State Law-- These laws and regulations are designed to protect the health & safety of humans and animals and to promote good stewardship for federal research funding…but they entail real costs for monitoring compliance
         a. Inventories
         b. Standardized accounting systems
         c. Record keeping and archive storage
         d. Certification programs
         e. Training programs
         f. Legal expenses
         g. Specialized facilities costs
         h. Hazardous waste storage and disposal
         i. Occupational safety and health,
         j. Animal care (IACUC)
         k. Human subjects protection (IRB)
   C. What is UAB’s IDC Rate?
      1. The current negotiated research rate for federally funded trials for 2003 is 45%
         a. DHHS is the federal agency that provides most of our federal funding and is responsible for negotiating the institution’s rate
         b. Rate is negotiated based on UAB’s validated, historical data, and is expressed as a percentage of allowable costs/direct cost base
         c. This rate represents less than the full share of IDC attributable to federally sponsored research
         d. For federally-funded clinical trials the negotiated on-campus indirect cost rate is 45%; the rate for off-campus trials is 24%
         e. Off-campus rates are lower than on-campus rates because facilities-related expenses can be built into the direct costs of off-campus federally-funded clinical trials and recovery of these costs cannot be duplicated via IDC recovery
2. For industry-sponsored clinical trials, the School of Medicine indirect cost rate of 19% is applied; some departments apply an additional percentage to cover departmental infrastructure.
   a. UAB’s indirect costs rate for industry-sponsored clinical trials is equal to or lower than those for many other private research institutions
   b. Range (24-29%)

D. Thinking of Requesting an IDC Waiver?
   1. Remember that the indirect costs of conducting clinical trials are REAL costs that must be recovered either through the IDC rate applied, or from School and/or Departmental funds
   2. IDC funds are NOT discretionary funds
   3. If IDC waiver requests are granted, there are fewer funds available for other School/Departmental initiatives
      a. Reimbursement of IDC represents a component of departmental L1 budgets
      b. The cost of doing clinical research is greater than what is recovered through indirect costs
      c. Revenue stream related to patient care is no longer sufficient to support uncovered indirect costs
      d. Regardless, the SOM is obligated to pay for all of its research activities

II. CONFLICT OF INTEREST DISCLOSURE, MANAGEMENT, AND AVOIDANCE
   A. School of Medicine Policies on Commitment, Private Consulting, and Other Extraordinary Contributions
      1. A full-time faculty member is bound to provide 100% of his/her professional effort to the School, University, and UAB medical practice plans.
      2. A faculty member may engage in private consulting up to 5% of his/her professional effort with the prior approval of the Chair, Dean, and must be disclosed to the Office of the Conflict of Interest Review Board (CIRB) at the time of submission of the Clinical Trial Contract to Grants and Contracts Administration (OCGA).
      3. The University of Alabama at Birmingham encourages external activities which enhance an employee’s value to UAB; which enhance UAB’s presence in the local, national, or international communities; or which provided public service. Such service to outside educational, professional, scientific, artistic, cultural, civic business, or other organizations is permissible under the terms of the policy. If this activity
poses a potential conflict of interest, review by the CIRB will be required.
The Conflicts of Interest Policy covers compensation received by faculty or other employees for consulting activities under UAB consulting guidelines.

B. School of Medicine Procedures on Start-up Companies and Similar Activities
   1. Faculty is required to submit to Chair and Dean a report outlining the business plan.
   2. Report must be reviewed by the UAB the Office of the Conflict of Interest Board and the Research Foundation.
   3. Employees of the University must disclose any conflicting interests in any transaction involving the University and they cannot use their personal influence in connection with, participate in, or act on the matter.

C. University Conflict of Interest Policy
   1. Any activity of employees engaging in any business or financial relationship, transaction, or event that may be viewed, internally or externally, as a conflict of interest between the employee and an outside party and that would result directly or indirectly in financial benefit including but not limited, monetary compensation, accruing to the employee. This includes, without limitation, contractors, consultants, vendors, suppliers, and others. All such activities must be disclosed to Office of the CIRB at the time of proposal submission to the OGCA.
   2. Provides several examples, including disclosure of the University’s non-public information for personal profit and acceptance of gratuities or special favors valued over $10,000 per annum for any combination of salary, payments for services, equity, income from intellect or property rights.

D. University Policies and Procedures for Faculty Members Involved in Sponsored Research and Technology Transfer
   1. Allows faculty, under appropriate circumstances and disclose to the Office of the CIRB, to hold equity in, serve as a board member or officer of, serve on a scientific advisory board of, and be the PI for research sponsored by a research sponsor or licensee of UAB technology.
   2. Applies to the investigator (his or her spouse and dependent children, parents, domestic partner, step parents and/or siblings including adoptive, half siblings and children related as a result of remarriage), co-investigators, and collaborators. Therefore, the investigator has a duty to report potential conflicts of all these individuals.
   3. Investigators who are involved in clinical trials must demonstrate that they are uniquely qualified to perform the trial.
a. Uniquely qualified means that the skills of the Investigator and the technology are such that no one else can do the activity and that the issue under trial is of such benefit to the public that an exception should be made.

E. Managing Conflicts – General Principles
1. UAB owns all the intellectual property generated by its employees and students (with some exceptions).
2. External activities cannot compromise the employee’s ability to perform his/her full-time UAB job.
3. UAB business (scholarship, teaching service) is conducted in a manner that is above inferences that the activity could be compromised by the employee’s expectation of financial gain, direct or indirect.
4. Students, trainees, and employees must be assigned duties consistent with their status and position. Their work should not be compromised by agreements with external sponsors or by a faculty member’s financial interests.
5. The University must authorize any use of UAB’s research facilities, personnel, and intellectual property for use by anyone other than UAB.

F. Process for Disclosure & Review
1. Disclosures obtained annually from faculty
2. Disclosure statements included on Sponsored Projects Approval Form and IRB and IACUC applications
4. Disclosures reviewed to determine whether a conflict of interest or commitment exists

G. Types of Information Requested for Review by COI Committee
1. Faculty status
2. Research proposal/business plan
3. Equity interest/financial interest
4. Corporate information
5. Consulting/Advisory Agreements
6. License Agreements
7. Leasing Agreements
8. Research Agreements
9. Intellectual Property where the Investigator is an inventor

III. OFFICE OF INTELLECTUAL PROPERTY MANAGEMENT (OIPM)
A. OIPM’s Mission – Identify, assess, market commercially biable intellectual property developed at the University of Alabama at Birmingham and Southern Research Institute (SRI)
1. Service to the UAB and SRI community
2. Enable access by the public to UAB inventions
3. UAB Patent Policy
   a. OIPM monitors/enforces the License Agreement
   b. OIPM initiates steps to protect rights of the discovery including the domestic and foreign patents.
   c. OIPM seeks, negotiates, manages and monitors licensing agreements on behalf of UAB and SRI
   d. OIPM ensures compliance to government regulations

B. Clinical Trial Agreements (CTAs): UAB retains rights to all inventions that it would own under U.S. Patent Law. UAB may grant a non-exclusive, royalty-free license to the Sponsor to use the invention. It may also grant a right of first refusal to the Sponsor to acquire an exclusive, royalty-bearing license.

C. Investigator-initiated Clinical Trials
   1. Greater probability of inventive activity on part of the UAB investigator (e.g., protocol provided by investigator, proposed new off-label uses) and thus UAB typically claims IP ownership rights in any agreement
   2. Study drug/device may be provided via an incoming Material Transfer Agreement (MTA), which typically has IP terms (OGCA negotiates MTAs)
   3. Possibility of government/foundation funding having IP “strings”
   4. Resolving IP issues in the Clinical Research Environment
      a. OGCA negotiates the terms of the CTA with the Sponsor (keeping investigator informed through OCGA Tracking Long entireties.
      b. Investigator should indicate (on the MTA Questionnaire) whether the MTA is a vehicle for obtaining a study drug/device for use in a clinical trial
      c. Investigator should submit an Invention Disclosure Form to UABRF for any invention discovered in the course of a clinical trial

IV. HIPAA PRIVACY AND SECURITY REGULATIONS ON CLINICAL RESEARCH
Note: This section gives general guidelines on HIPAA requirements and will be updated as the Office of Research Compliance formulates specific HIPAA guidelines for UAB researchers in 2003. Please go to the HIPAA website for more information (www.hrm.uab.edu/HIPAA/home.html).

A. Main objectives of the Privacy Rule
   1. Inform patients of how their protected health information will be used.
   2. Establish the conditions for the use of Protected Health Information (PHI) by covered entities for research and the disclosure of PHI by covered entities to researchers.
   3. Place conditions that must be met for the use and disclosure of PHI information for research purposes.
   4. These conditions are intended to supplement those required under the Common Rule and FDA regulations.
B. Privacy and Clinical Research
   1. HHS states - Benefits of research must be balanced against the risks, including privacy risks, for those who participate in research. An individual’s rights and welfare must never be sacrificed for scientific or medical progress.
   2. HHS states - They believe that the use or disclosure of individual identifiable health information to a researcher posed the greater risk to individual privacy, not publication of de-identified information.

C. Patient Authorization:
   1. If a researcher is to have direct contact with the research subjects, the researcher should in virtually all cases be able to seek and obtain the patients’ authorization for the use and disclosure of protected health information about themselves for the research study.
   2. If the researcher obtains a waiver of authorization then the researcher must ensure that the protected health information will not be re-used or disclosed to any other person or entity except as required by law, for authorized oversight of the research project, or for other research for which the use of disclosure of PHI would be permitted.
      a. The authorization form requires an “expiration date” – while this may be impractical, the rule requires it. However, you may use a statement like “for the duration of a specific research study.”
      b. An authorization can be revoked. Once revoked no additional PHI may be used or disclosed by the covered entity. Covered entity can continue to use PHI disclosed prior to revocation as appropriate to preserve the integrity of the research study. To do otherwise would undermine the primary objective of the authorization requirement to be voluntary, informed choice of the individual.

V. JAMES A. PITTMAN GENERAL CLINICAL RESEARCH CENTER (GCRC).
   A. GCRC Study Categories
   1. Category A: Patients admitted to GCRC for research purposes only on an investigator-initiated study protocol. All costs (up to GCRC Advisory Committee (GAC) -approved ancillary costs limit) paid by GCRC grant.
   2. Category B: Patients admitted to GCRC for diagnosis and treatment, but participate in a GCRC research protocol. Room and board and costs of routine care billed to patient/insurance; costs of services performed for research paid by GCRC grant.
   3. Category C: Patients admitted to GCRC for diagnosis and treatment and do not participate in a GCRC research protocol. All costs billed to patient/insurance. Examples include routine pre-op evaluations, dynamic endocrine testing. No charges paid by GCRC grant.
4. Category D: Patients admitted to GCRC on industry-initiated study protocol (clinical trial). The Principal Investigator puts the GCRC costs into his/her budget to industry. All costs then paid by industry via the University account number of the P.I.

B. Procedures for Clinical Trial Research at the UAB GCRC
   1. Initial discussion of protocol with GCRC Administrator, Program Director and RSA Faculty
   2. P.I. submits protocol, GCRC form pages, Data Safety Monitoring Plan (DSMP), biosketches to GAC
   3. P.I. submits protocol to the IRB (can be concurrent with GCRC submission)
   4. Roundtable discussion with GCRC staff after both IRB and GAC final approval

C. Clinical Trial Research in the GCRC
   1. Cover page with project title and academic titles of investigators
   2. Biosketches and active/pending Other Support of key personnel
   3. Research Plan (ideally in 5-page format)
      a. Hypothesis and Specific Aims (1/2 page)
      b. Background and Significance (1 page)
      c. Preliminary studies (1/2 page)
      d. Research Design and Methods (3 pages)
   4. Gender and Minority Tables; Human Subjects (PHS 398 format),
   5. Data Safety Monitoring Plan (or DSMB as indicated)
   6. Literature Cited
   7. Consortium/contractual arrangements, consultants
   8. Justification for use of GCRC
   9. Attachments (budget, use of Core Lab and Bionutrition Units)
   10. Day to day protocol (essentially study orders to GCRC staff)

VI. DEPARTMENT OF BIOSTATISTICS - BIOSTATISTICAL CONSULTATION & COLLABORATION.
   A. Biostatistics Consulting Center Services
      1. Offers comprehensive statistical consultation and collaboration.
      2. Review research needs and study design issues
         a. Estimate workload
         b. Establish timetables
         c. Cost estimate

VII. GUIDELINES FOR MANAGEMENT OF INVESTIGATIONAL DRUGS
   A. Control of Investigational Drugs
      1. Administer drugs only to study subjects under investigator’s personal supervision
      2. Do not supply to any person not authorized to receive investigational drug
3. Maintain adequate records of disposition
4. Return supplies of drug to sponsor or provide for alternative disposal

B. Record Keeping and Record Retention
   1. Maintain adequate records of drug receipt and drug dispensing
   2. Maintain records of drug disposition when study is closed
   3. Retain all accountability records

C. Disposition of Unused Supply of Investigational Drug
   1. Sponsor assures return from each investigator
   2. Sponsor may authorize alternative disposition
   3. Sponsor maintains written records of drug disposition

D. Drug Accountability Issues
   1. Storage
   2. Required record keeping
   3. Controlled use
   4. Transfer from location to location
   5. Expiration dating
   6. Accountability and reconciliation

E. Services Provided to Insure investigational agents are handled safely, effectively and efficiently in the hospital and clinic environment
   1. Maintain drug inventory and accountability records
   2. Dispense investigational drugs to inpatients and outpatients
   3. Prepare blinded doses for double-blind trials
   4. Conduct randomization for blinded studies
   5. Prepare randomization code for investigator-initiated studies
   6. Interact with study sponsor on all aspects of drug control
   7. Provide drug information to staff handling investigational drugs

VIII. THE ROLE OF THE OFFICE OF GRANTS AND CONTRACTS ACCOUNTING.
A. The Office of Grants and Contracts Accounting is the “post-award” office for all sponsored agreements. Its primary functions are:
   1. Sets up the account and budget after OGCA approval
   2. Financial accounting and reporting
      a. Monthly financial reports to the PI and the department
      b. Monitor individual accounting transactions for any university or sponsor compliance requirements for restrictions.
      c. Submit W-9 and other tax letters or financial documents to the sponsor (as requested)
   3. Receive and deposit payments into the accounting system. (All payments come directly to the department.)
4. Contact for sponsor and other audits
5. Assist PI/Dept. in oversight of the ongoing status of budgets and monthly accounting transactions.
RELATED WEB ADDRESSES AT UAB

http://main.uab.edu/show.asp?durki=55757  For information on Clinical Trials through the Office of Research Compliance

http://main.uab.edu/show.asp?durki=30246 - For information on the IRB

http://main.uab.edu/show.asp?durki=30265 – For information on Office of Grants and Contracts Administration

www.health.uab.edu/insight  - For information on advertising your trials on the UAB website

http://main.uab.edu/show.asp?durki=55753 - For information on Research Policies


http://main.uab.edu/show.asp?durki=30255 – For information on faculty matters such as Conflict of Interest Disclosure, Management and Avoidance; Procedures on Start-up Companies; and Consulting Agreements

http://main.uab.edu/show.asp?durki=30261 - For additional information on Conflict of Interest and other Research Policies at UAB

http://main.uab.edu/show.asp?durki=34763  - For information on the James A. Pittman GCRC

http://www.soph.uab.edu/bsthome.asp?ID=15  – For information on the Department Biostatistics

http://main.uab.edu/show.asp?durki=1032  – To access the Financial Affairs web page

http://www.hrm.uab.edu/HIPAA/home.html - For information on HIPAA

http://www.uab.edu/uasom/research/  - School of Medicine research website

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Appendix A

Assessing a Clinical Trial Budget
How to Determine Financial Feasibility of a Clinical Trial from a Sponsors Budget

Practical Tips

These tips provide a good benchmark for you when deciding if a study is financially feasible. They apply to medical trials that are Phase III, Multicenter, Pivotal trials of approximately 6 months in duration.

- The amount of funding per patient initially offered by a sponsor is one quarter to one third less than the amount of funding required to conduct the study and keep the study fiscally sound.

- Per patient funding: an average is $8,000 - $11,000 per patient (includes indirects); more if intensive procedures are involved (safety, monitoring, surgery, inpatient procedures, etc.)

- For an 18 – 24 month study, usually 65-80% of the budget is spent in the first year. (This is for a 6 month, blinded, efficacy, Phase III trial with an enrollment phase of a year.)

- Usually 75% or more of a budget is effort (salary).

- For most studies, 20-40% (30% average) of a research coordinator’s time is required; more for surgery studies and studies requiring complicated procedures (up to 100%).

Note: This is a guideline only for Phase III, Multi-Center, Pivotal medical trials. Studies can vary widely in labor intensity, duration, procedures, safety, etc. It is important that you develop your budget based on the Sponsor’s Schedule of Assessments and protocol.
Appendix B

“Hidden” Effort: Beware of Effort not Included in Sponsors Budgets: A Description

What is “Hidden” Effort? Hidden effort is effort or labor that is not usually expressed in a sponsor’s line item budget as a procedure, but is true effort just the same. Also, most line item budgets are too low because they do not fund “hidden effort” well if at all. Some examples of hidden effort:

**Investigator:**
- Assess and learn the protocol.
- Assess sponsor’s budget.
- Negotiate costs with other departments.
- Create an Internal Budget.
- Consent the patient.
- Read and interpret labs, x-rays, videotapes, etc.
- Oversee serious adverse events.
- Confer with the coordinator, the sponsor, and other colleagues on occasions other than during the study patient visit.

**Research Coordinator:**
- Learn the protocol.
- Educate the patients on study procedures.
- Consent the patient.
- Take telephone calls from patients.
- Handle adverse events and process the paperwork for them.
- Completing Case Report Forms and other patient documentation.
- Handle regulatory documentation.

**Administrative Assistant/Finance Manager:**
- Format informed consent and submit IRB package.
- Handle regulatory documentation including amendments, renewals and correspondence.
- Oversee financial management.

The sponsor’s line item budget should be negotiated when the budget is too low to cover costs. Line items can be added to the sponsor’s budget with descriptions such as:

Investigator Fee, Coordinator Fee, Administrative Fee, Informed Consent, and Adverse Events
Appendix C

BUILDING AN INTERNAL BUDGET FOR CLINICAL TRIALS

The Issue of Effort (Salary):
How to Manage Salary throughout the Course of a Clinical Trial

The Biggest and most Variable Expense on most Clinical Trials is Effort (Salary), usually comprising 75% or more of the Budget.

Variables which effect % salary effort:

- Sponsor withdraws study before study starts. However, start-up costs have been incurred i.e., IRB submission packet.
- Sponsor delays study once it is funded. Thus, funding is not being earned, but salaries are being paid from the study.
- Sponsor withdraws study in the middle of it.
- Enrollment does not meet expectation due to difficulty in recruiting patients. Thus, funding is less than anticipated.
- For studies short in duration, a study has often been completed by the time the correct salary is applied to the study.
- Amount of time required by research coordinator or investigator to treat patients is far greater/far less than expected.

Therefore:

- Salary should not be placed on a clinical trial account until patients are actually being seen.
- Salary (% effort) should be evaluated at least every 3-6 months.
- The internal budget is a valuable guide regarding how % effort will be played out for each employee on each study. However, because of the nature of clinical trials, effort (salary) can and will change during the course of the study.