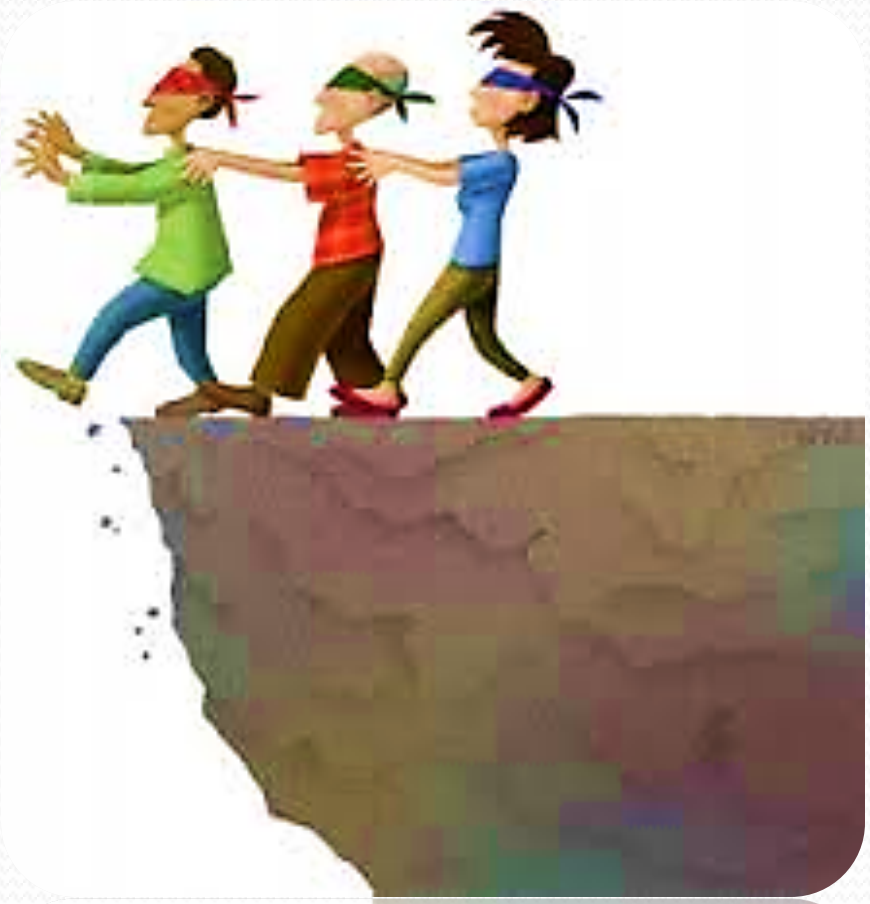
Clinical Trials: Understanding the Mad, Mad World of Building and Negotiating Clinical Trial Budget

Jeff Moore, PhD
Cleveland VA Medical Research
and Education Foundation

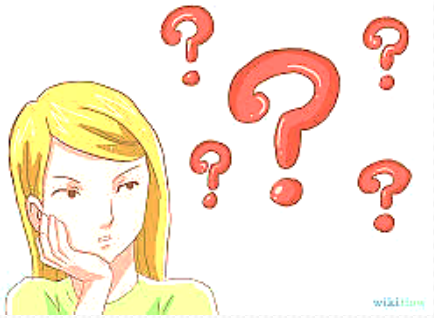
Does Budgeting Make You Feel Like This?



Four Main Components of Clinical Trial Budgets

- Start up Fees
- Budget
- Negotiations
- Payments

Choosing to Participate in a Clinical Trial



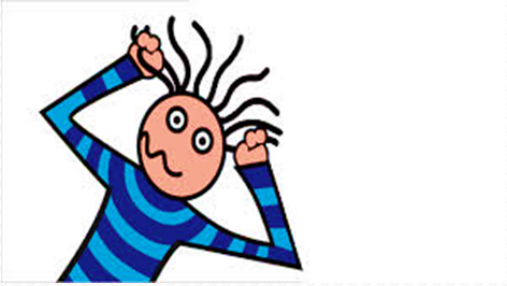
- Does the study have scientific merit?
- Will the proposed budget support the staff required?
- Is the population to be studied obtainable at the VA?
- Are there studies at the VA competing for the same population?
- Is there space/resources to perform the work required?

Direct vs Indirect Costs

Direct

Costs directly related to the performance of the research

- Personnel
- Supplies
- Equipment
- Lab Costs



Indirect

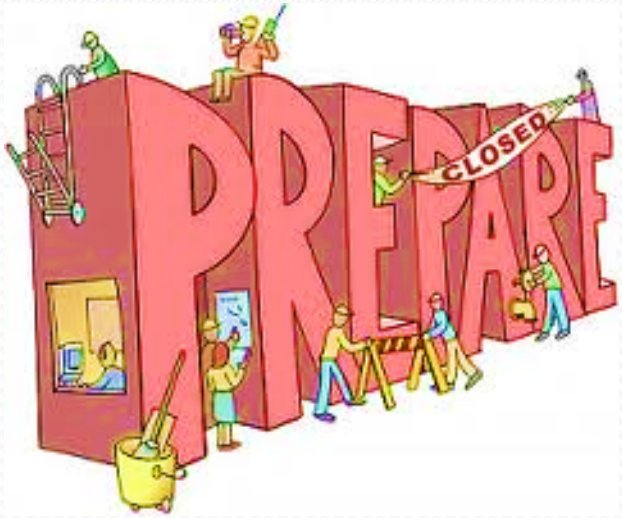
Costs not directly related (institutional overhead)

- Research Space
- Equipment Upkeep
- Utilities (phone, copier, fax electricity)
- Accounting and Payroll
- Overhead/Indirect rate is 25% for foundation

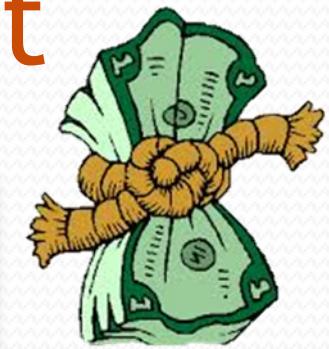
Study-Start Up

All the Activities Required BEFORE the First Patient

- Review of the Protocol
- IRB Fees/Regulatory preparation
- Preparing for site initiation visit
- Sponsor Meetings
- Pharmacy Set-Up



Sample Start-Up Budget



START UP Costs	Total
Investigator Protocol Review	500
Site Initiation Visit	500
Regulatory Documents and IRB Preparation	1,000
Source Document Preparation	1,000
Advertising	5,000
IRB Fees	2,000
Pharmacy Set-up Fee	750
Staff Training	1,500
Total	12,250

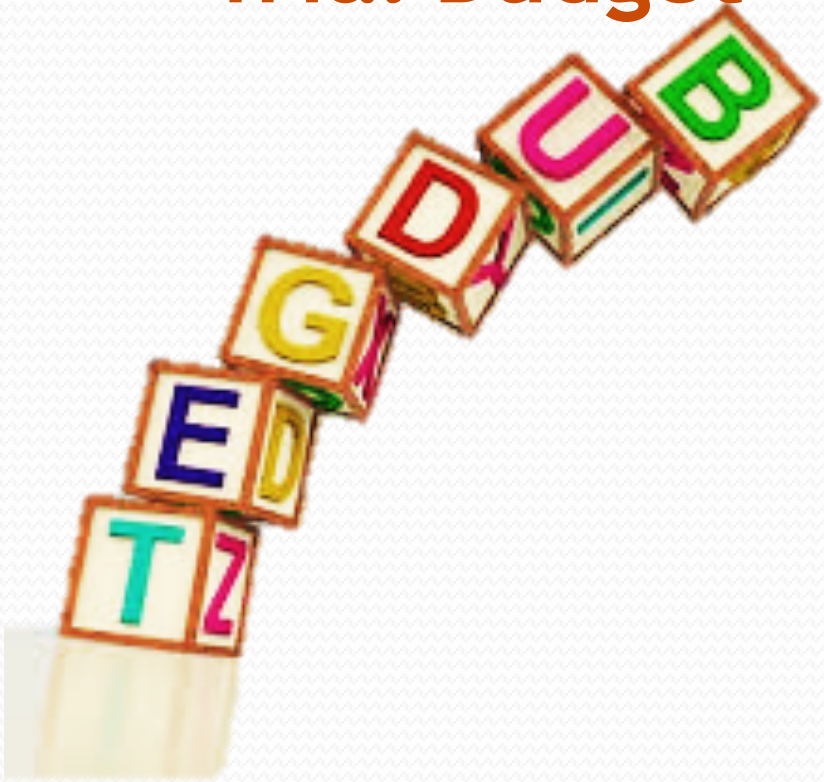
Fees should be "fair market value". The expenses incurred BEFORE subjects are enrolled

Start up Fee Worksheet

Role	Hourly Rate	Comments	Rates with Fringe
Primary Investigator	$ 241		$ 313.30
Research Coordinator	$ 50		$ 65.00
Contracts Department	$ 52		$ 67.60
Regulatory Department	$ 52		$ 67.60
General Counsel	$ 200		$ 260.00
Overhead Rate:	0%	25%	

Activity / Service	Role (drop down)	Center Estimated Time
Protocol Review	Primary Investigator	2.00
Protocol Review	Research Coordinator	3.00
Budget Review	Contracts Department	1.00
Budget Negotiation	Contracts Department	2.00
Clinical Trial Agreement Review	Contracts Department	2.00
General Counsel Review and Approval	General Counsel	2.00
Clinical Trial Agreement Negotiation	Contracts Department	0.00
Critical Study Documents Completion/Sponsor Correspondence	Regulatory Department	4.00
Informed Consent Review	Research Coordinator	2.00
Informed Consent Negotiation	Research Coordinator	4.00
IRB Preparation for Submission/Correspondence with IRB	Research Coordinator	25.00
IRB Meeting Attendance	Primary Investigator	0.50
IRB Meeting Attendance	Research Coordinator	0.50
Protocol Training	Primary Investigator	1.00
Protocol Training	Research Coordinator	2.00
Other		
Total Start-up (Includes Overhead)		**$ 4,665**

Building Your Clinical Trial Budget



Review the Protocol

Utilize the Visit Schedule

	VISIT 1 Screening	VISIT 2 Run-in	VISIT 3 Randomization	VISIT 4 Month 3
Informed Consent	X			
Medical History	X			
Complete Physical Exam	X			
Concomitant Medication review	X	X	X	X
Height	X	X	X	X
Weight	X	X	X	X
Vital Signs	X	X	X	X
Waist Circumference	X	X	X	X
A1c	X	X	X	X
ECG		X		
Pharmacy Dispensing	X			X
Patient Reimbursement	X			X

Assign a Cost to Each

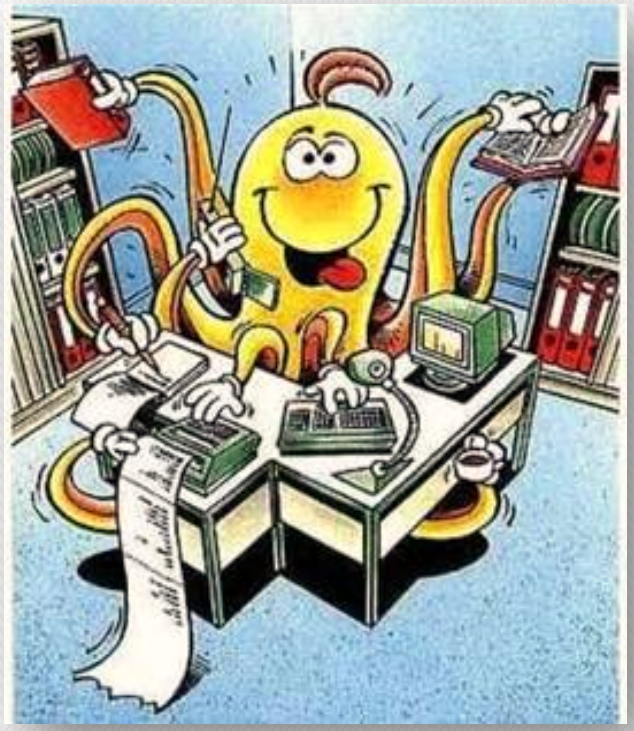
	Hourly Fee	Fringe	Total
PI Fee			
Coordinator			
Research Asst			
Lab Tech			

	Visit 1 Screening	Visit 2 Run-in	Visit 3 Randomization	Visit 4 Month 3
Informed Consent	x			
Medical History	x			
Complete Physical Exam	x			
Height	x	X	X	X
Weight	x	x	x	x
Vital Signs	x	x	x	x
Waist Circumference	x	x	x	x
A1c	x	x	x	x
ECG		x		
Concomitant Medication Review	x			X
Medication Dispensing	x			x

This method provides an accounting of the time intensity of each procedure

Actual Examples of Budgets

Consider Required Activities Not in the Visit Schedule



- Adverse Event Processing
- Queries
- Monitoring Visits
- Retention
- SOP Development
- Amendments
- Unscheduled Visits
- Management of Reg Binders

Additional Considerations

- Where will the lab analysis be performed?
- Will the PI need to interpret results (e.g. ECG's)?
- Will subjects need transportation money or parking?
- Subject Reimbursement
- Will the sponsor provide equipment?

Invoiced/Pass-Through Expenses to Consider

Invoiced Items/Pass through Expences:		Cost
Screen Failures		0
CONTINUING REVIEW/AMENDMENTS each		$500
RECORD RETENTION (PER PARTICIPANT)		$75
Unscheduled Visits		Upon invoice
MES/SAE		Upon invoice
Dry Ice		Upon invoice
Queries		Upon invoice
Monitoring Visits		Upon invoice

Common Pitfalls

- Underestimation of Staff Time Required for Activities
- Overestimation of the Number You Can Recruit
- Overlooking the Invoiceable items
- Fragmentation of Staff
- Taking on a trial without a strong coordinator or experienced staff

Research Coordinator: you get what you pay for

- Cost of a coordinator?
  - 35K to 100K per year

- Lower cost for primary coordinator = higher cost of oversight

- Value of a good coordinator?

  Priceless

Negotiating the Budget

- Past performance/relationships can have a positive influence on current negotiations
- Sponsors want trial to be successful and are willing to negotiate reasonable requests
- Remember: ***You can re-negotiate after trial starts***

Commonly Missed Costs

- Actual time for consent process
- Screening for accrual
  - Screen failures, chart review, outreach
- Supplies and expenses necessary for the trial
  - Office supplies
  - Photocopying charges
  - Computers, phones
  - Equipment- ECG machine, camera
- Pharmacy costs

Commonly Missed Costs

- Lab costs
  - Equipment- freezer, centrifuge
  - Temporary storage of samples for send out
  - Long term storage for trial records
  - Labor needed to pack & ship
  - Shipping costs
  - Dry ice
- Repeat visits/cycles
- Follow-up visit contingencies
- PI conference calls
- Assembling patient binders and other Sponsor supplied materials
- Quality-of-life surveys and phone calls they may require
- Enrollment log completion and submission
- Study team meetings or procedures & events requiring more than one staff member for execution

Common Mistakes

- Overestimating the ease of obtaining subjects
- Under-budgeting for the unexpected
- Overestimation of research staff efficiency
- Failure to recover study start up costs
- Failure to include “possible” or “invoiceable” costs in initial budget

Tips for Success

- Know your “break-even point” and “bottom line” before submitting the budget
- Use the protocol schedule and timelines in planning
- Identify staff members to be involved BEFORE agreeing to a clinical trial
- Utilize all your resources and expertise of colleagues
  - Within the Medical Center
  - **And with other NPCs!!!!!!!!!!!!!!!!!!!!!!**

Other Factors for a Successful Clinical Trial

- Ease of Budget/Contract Negotiations and Finalization/ CRADA approval/Signatures
- Complexity of Protocol
- Investigator and Sponsor Responsiveness
- IRB and R&D committee approval time
  - CLE VAMC pre IRB review committee
  - Hired a full time regulatory specialist to handle IRB submissions
- Lengthy times for approvals can spell the demise of the clinical trial

Payments

- Per Patient

  Automatic vs invoiced

- Installments/Milestones

  Might be based upon enrollment

- Hold Backs

All payments under this Appendix shall be made on a quarterly basis, provided twenty percent (20%) of each payment will be retained to be paid in accordance with the Final Payment as outlined herein. Company will retain no more than $30,000.00. Once the holdback amount of $30,000.00 has been met, all ongoing payments will be paid at 100%.

Payments – Based Upon Enrollment

Payment Schedule

Total Number of Patients	90
Total budget amount (in local currency)	$172,036.71

The Grant shall be due and payable as follows:

1st Payment: $ 43,009.18 (or _25_ % of the total Grant) upon complete execution of this Agreement, receipt of Institutional Review Board approval and confirmation clinical trial databank registration on www.clinicaltrials.gov*.

2nd Payment: $ 43,009.18 (or _25_ % of the total Grant) upon receipt of satisfactorily completed quarterly Status Update (Exhibit D) indicating the __50__% milestone has been achieved. **Paid based on actual enrollment of evaluable subjects _1_ through _45_

3rd Payment: $ 34,407.34 (or _20_ % of the total Grant) upon receipt of satisfactorily completed quarterly Status Update (Exhibit D) indicating the 100% enrollment milestone has been achieved. **Paid based on actual enrollment of evaluable subjects _46_ through _90_

4th Payment: $ 34,407.34 (20% of the total Grant) upon receipt of a manuscript quality final report to Merck. (Merck committee review required prior to final payment release)

Final Payment: $ 17,203.67 (10% of the total Grant) upon verification of Final study results posted on clinicaltrials.gov.

NPC Lead Multisite (Master): Case study

- CVAMREF lead for Pfizer study
  - Recruited all 19 VA sites
  - Negotiated Budget for ALL sites
  - Prepared IRB submission for VA C-IRB
  - Worked with each local VA to submit LSI (Local Site Investigator)

Lessons Learned: Lead NPC Multisite

- Be sure of what you are getting into!!
- Staffing/Resources
  - ED time, grant/budget person time, IRB person's time
- Communication!!!!
  - Industry Partner, NPCs and VA C-IRB
  - Set realistic timeframes
- Payment for being the lead
  - Make sure you figure this into your local budget

Questions?