Essential Budgeting Requirements for Conducting Clinical Research

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Agenda/Learning Objectives

- LOI/CDA
- Developing Study Budgets
  - Things to Consider When Creating a Clinical Trial Site Budget
  - Research vs. Standard of Care
  - Common Budget Mistakes & Hidden Costs
- Clinical Trial Agreements
- Financial Management

Letter of Intent

- A letter of intent is used to express interest in being part of a specific study
  - Confirms available facility, staff & patient population
- Typically will require institutional & investigator sign off
- If LOA is required, needs to be in place in order to receive the CDA

Confidential Disclosure Agreement

- A C.D.A. is a legal contract that governs the exchange of proprietary or confidential information. The agreement is used when there is a need to share proprietary information with an external party for a limited purpose while protecting it from being disclosed to others or the public.
  - Needs to be in place in order to receive the study protocol

Study Feasibility Questions

- Understand the protocol, the required procedures and scope of work involved
  - Is this clinical trial compatible with your research program?
  - Are the requirements of the clinical trial reasonable?
  - Is the patient population available?
  - Are the inclusion/exclusion criteria to narrow?
  - Is there appropriate study staff available to properly conduct the study?

- You've decided to participate!

- You need a budget…

Why Bother to Budget?

Purpose of Developing Budget

- Understand the cost
- Identify who will pay for what
- Identify hidden cost
- Documentation of cost
- Identify Research Related vs Standard of Care
- Informed Decision

Developing Study Budgets

- Developing Clinical Trial Study Budgets serves two primary purposes
  - Ensuring sufficient funds are available to perform the study start to finish
  - Identifying procedures that are research-related and must be billed to the grant account vs. Standard of Care and billable to the subjects insurance

Developing Study Budgets

- Carefully Review the Protocol – including any footnotes in SOA
- Input from Investigator, coordinator, sponsor
- Provide Justification for Start up fees
- Ask for more than you think you need
- Know institutional requirements – finance and compliance

Under budgeting will result in fund deficit regardless of recruitment

Developing Study Budgets

- **<u>Remember</u>:**

  Every company, every protocol is different

Things to Consider When Creating a Clinical Trial Budget

- Salary Support – Time & Effort for all study activities

  Study staff time is the primary factor to the high cost of conducting clinical trials and is frequently underestimated

  - PI & Co-Investigator
  - Other Specialty Physicians (Ex. Anesthesiologist)
  - Research Coordinator – Research Nurse
  - Data Coordinator (Data Entry; Query Resolution)
  - Research Pharmacist
  - Other

Calculating Time and Effort is one of the most difficult parts of the budget.

Things to Consider When Creating a Clinical Trial Budget

Coordinator Responsibilities – Time & Effort

Examples:

- Regulatory Documents
- Scheduling
  - Visits & procedures/tests/scans
- Screening
- Consent
- Data Entry/CRFs
- Query Resolution
- Study Monitor Visits
- Subject Follow up
- Subject Payments/Reimbursements
- Adverse Events
- Conference Calls/Meetings

Coordinators have a lot of responsibilities

Make sure their time & effort is covered

Things to Consider When Creating a Clinical Trial Budget

- Study Related Supplies
- Regulatory Binders
- Conference Calls, Webinars
- Overnight Shipping/Postage
- Correct Lab/Procedure Charges
  - Research Rate
  - Use specific CPT Code
  - Include future charge increases
  - Include professional fees
- Study Initiation & Close out Meetings
- Specialty Training Costs
- Drug/Device Costs
- Subject Compensation
- Study Monitoring
- Hospital Room Charges/clinical fees
- Site Research Pharmacy & Dispensing
- Central Pharmacy / Central Lab

Things to Consider When Creating a Clinical Trial Budget

- Invoiceable Costs (Pass Thru Costs)
  - Chart Review
  - IRB/WIRB Fees – Initial, Amendments & Annual Renewals
  - Protocol Amendment Preparation
  - AE/SAE Management
  - Safety Reports
  - Audits – Time & Effort of Study Team
  - Screen Failures
    - Quantity allowed
    - Amount Per Screen Fail
  - F&A on above

- Invoiceable Costs (Pass Thru Costs) Continued
  - Shipping of Samples – packaging & Dry Ice
  - Travel to Subjects for Visits
  - Medicare Coverage Analysis
  - Study Staff Time with Study Monitor
  - F&A on above

Things to Consider When Creating a Clinical Trial Budget

- One Time Costs
  - IRB Preparation
  - Recruitment/advertising Costs
  - Pharmacy Review and Set-up Fees
  - Document Translation Costs
  - Publication Fee
  - Administrative Start-up - whether or not you enroll any subjects
  - Close-out Fees
  - Device/Equipment Purchase (Freezer)
  - Long Term Document Storage

    - Be sure to include F&A Costs

Things to Consider When Creating a Clinical Trial Budget

Budget for Document Storage/Archiving/Record Retention Fee

Invoiced at end of Study

$100 Per Month

24 Months (2 Years)

$2,400 + F&A

Store each study separately

Example above includes: Initial Fees, Supplies & Monthly Fee for 20 Boxes

Record Retention

- 21 CFR 312.62 FDA - Investigational New Drug
  - FDA Regulated – Investigational drug or device: 2 years after the investigation is discontinued and FDA notified, following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or the application is not approved for such indication
    - **Confirm with institutional policy**

Things to Consider When Creating a Clinical Trial Budget

- **Payment Schedule**
  - Start-up costs
    - Non refundable – Internal paperwork & study set up
    - Due upon execution of Clinical Trial Agreement
  - IRB Fee
    - Administrative Non Refundable Fee
    - Invoiced with Start-up Costs
  - Advance subject fee for the first subject enrolled
    - To assist in cash flow – credit toward future payments
    - Due upon execution of Clinical Trial Agreement

Absence of start-up costs usually results in a deficit fund balance for the life of the study

  - Payment Schedule – Meet institutional policy
    - Quarterly; Annual; After Monitor Visits

Things to Consider When Creating a Clinical Trial Budget

- Re-Negotiation is an Option
  - If the Protocol is amended….
    - If the amendment changes work scope or adds procedures – re-negotiate
  - If the sponsor allows more patients to be enrolled, request more screen failures

Guidelines for Developing Budgets

- Develop a Realistic Budget
- Justify your needs
- Keep it Reasonable

Remember – Everything has an expense

"You name it. I'm collecting for it."

Guidelines for Developing Budgets

- One size does not fit all. Customize budgets taking local realities and study complexity into consideration
- Never agree to the Industry Sponsor's initial offer no matter how incredible the dollar amount sounds without a thorough analysis of the specific protocol
  - Sponsors have a plan to make money
  - Don't let aggressive Sponsors push you around – Use your Institution resources to help with negotiations (Good Cop vs. Bad Cop)

Remember – Everything has an expense

Guidelines for Developing Budgets

- If it's not in the contract you are not guaranteed to be paid
- If you don't ask for it, you won't get it

Remember – Everything has an expense

Guidelines for Developing Budgets

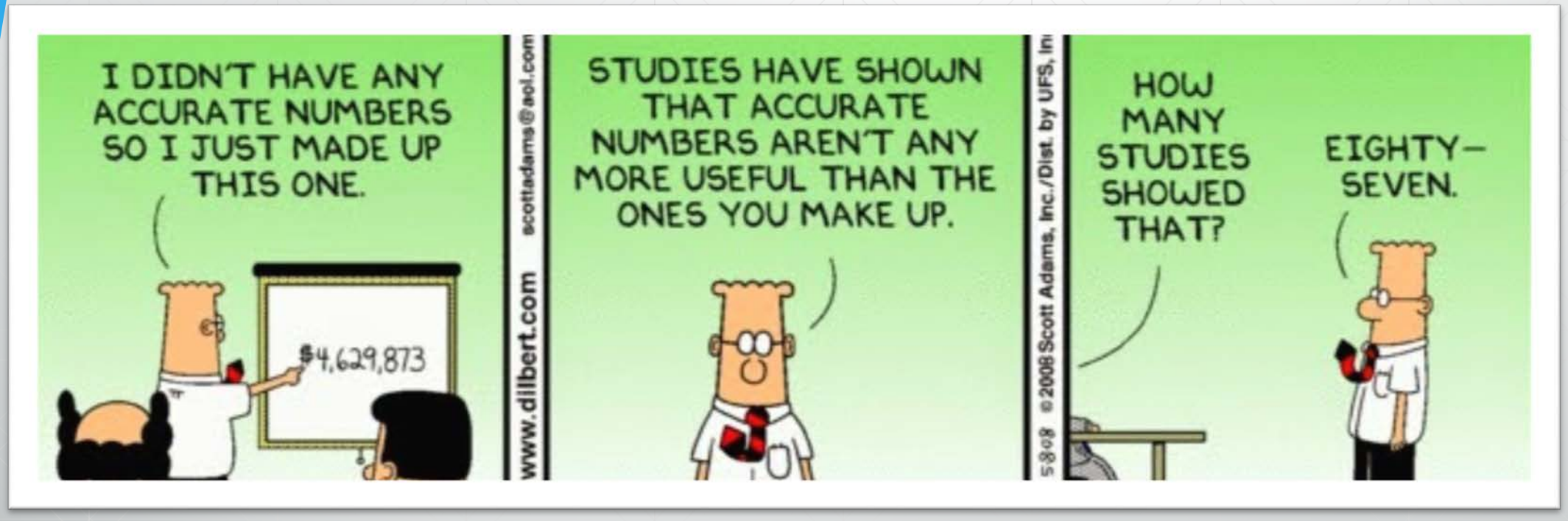
- Fair Market Value

"The fair market value is the price at which the property would change hands between a willing buyer and a willing seller, neither being under any compulsion to buy or to sell and both having reasonable knowledge of relevant facts."

United States Supreme Court decision in the United States v. Cartwright

Guidelines for Developing Budgets

- Fair Market Value
  - Payment set at what the market will bear is in accordance with being able to defend the payment
  - Most institutions now have a FMV policy in writing to defend their actions and to prove transparency


I DIDN'T HAVE ANY ACCURATE NUMBERS SO I JUST MADE UP THIS ONE.
$4,629,873
www.dilbert.com scottadams@aol.com
STUDIES HAVE SHOWN THAT ACCURATE NUMBERS AREN'T ANY MORE USEFUL THAN THE ONES YOU MAKE UP.
5-8-08 ©2008 Scott Adams, Inc./Dist. by UFS, Inc.
HOW MANY STUDIES SHOWED THAT?
EIGHTY-SEVEN.

Research Related vs. Standard of Care

- Research Related vs. Standard of Care
  - Determine if each procedure is RR or SOC – Medicare Eligibility
  - Medicare Coverage Analysis
  - Investigator must carefully identify usual and customary care procedures vs. research specific procedures
    - A Medicare Coverage Analysis (MCA) is an analysis document that identifies and analyzes who the appropriate payer (Sponsor, Medicare, or other third party payor) is for each item and service required by the clinical trial protocol and schedule of activities.

Research Related vs. Standard of Care

- Research Related vs. Standard of Care
  - Research specific procedures would likely not be performed if the patient were not in a research study
  - Can not bill insurance for any item that is reimbursed by sponsor

Research Related vs. Standard of Care

- Research Related vs. Standard of Care
  - Usual and customary care procedures (SOC) would likely be performed if the patient was not in a research study
  - Route care tests and results may be used for research

Research Related vs. Standard of Care

- Research Related vs. Standard of Care
  - The sponsor may decide to cover all study related costs including anything that could be considered standard of care which would likely eliminate any need for third party billing.
    - Check with your institutions MCA Analyst

Research Related vs. Standard of Care

- Identify procedures and tests that are research and standard of care during budget development and clearly note on the budget.

Schedule of Activities

Activity		Screening Visit	Baseline Visit	Visit 1	Visit 2	Visit 3	Visit 4 (Telephone Visit)	Final Safety Visit (For early study drug discontinuation only)
Written Informed Consent	PI/CRC	X						
Inclusion/Exclusion Review	PI/CRC	X						
Medical History	PI	X						
Reproductive History	PI	X						
Demographics	CRC	X						
Subject History	PI/CRC	X						
Diagnosis	PI	X						
Physical Examination/Weight	PI/CRC	X						
Vital Signs/Height	CRC	X	X	X	X	X		X
12-Lead ECG	PI	X		X		X		
Safety Labs	PI	X						
Concomitant Medication Review	CRC	X	X	X	X	X	X	X
Adverse Event Review	PI/CRC	X	X	X	X	X	X	X
Randomization	CRC		X					
Administer/Dispense Study Drug	PI		X		X			
Drug Accountability/ Compliance	CRC			X		X		X
Subject Stipend			X	X	X	X		X

Per Subject Fee

Activity		Screening Visit	Baseline Visit	Visit 1	Visit 2	Visit 3	Visit 4 (Telephone Visit)	Final Safety Visit (For early study drug discontinuation only)	
Written Informed Consent	PI/CRC	$450.00							
Inclusion/Exclusion Review	PI/CRC	$250.00							
Medical History	PI	$300.00							
Reproductive History	PI	$200.00							
Demographics	CRC	$200.00							
Subject History	PI/CRC	$150.00							
Diagnosis	PI	$150.00							
Physical Examination/Weight	PI/CRC	$350.00							
Vital Signs/Height	CRC	$75.00	$75.00	$75.00	$75.00	$75.00		$75.00	
12-Lead ECG	PI	$250.00		SOC		SOC			
Safety Labs	PI	$450.00							
Concomitant Medication Review	CRC	$200.00	$200.00	$200.00	$200.00	$200.00	$200.00	$200.00	
Adverse Event Review	PI/CRC	$250.00	$250.00	$250.00	$250.00	$250.00	$250.00	$250.00	
Randomization	CRC		X						
Administer/Dispense Study Drug	PI		$200.00		$200.00				
Drug Accountability/ Compliance	CRC			$250.00		$250.00		$250.00	
Subject Stipend			$100	$100	$100	$100		$100	
Direct Cost Per Visit		$3,275.00	$825.00	$875.00	$825.00	$875.00	$450.00	$875.00	
Indirect Cost Per Visit 25%		$818.75	$206.25	$218.75	$206.25	$218.75	$112.50	$218.75	
TOTAL PER VISIT		**$4,093.75**	**$1,031.25**	**$1,093.75**	**$1,031.25**	**$1,093.75**	**$562.50**	**$1,093.75**	**$10,000.00**

Budget

- CTA states enroll up to 10 Subjects
  - 10 Subjects x $8,000 Per Subject Fee = $80,000 direct cost budget
  - Add F&A Costs – Industry Sponsored Clinical Research Rate – 25%
  - $80,000 + 25% = $100,000

Budget

- $100,000 Budget
  - PI Salary & Fringe
  - Research Nurse Salary & Fringe
  - Research Study Coordinator Salary & Fringe
  - Supplies
  - Ancillaries (Procedures)
  - 25% F&A Cost

Budget – How will you spend funds?

FUNDING AGENCY:	Corporate Sponsor				
NAME OF INVESTIGATOR:	Principal Investigator				
STUDY PERIOD:	1/1/2019 Through 12/31/2019				
Project Title:	Industry Sponsored Clinical Trial				
Personnel Name	Percent Effort	Base Salary	Salary Requested	Fringe*	Total
PI	5%	$192,300	$9,615	$3,365	$12,980
Research Nurse	15%	$95,100	$14,265	$4,993	$19,258
Research Coordinator	35%	$66,500	$23,275	$8,146	$31,421
	0%	$0	$0	$0	$0
	0%	$0	$0	$0	$0
Total Personnel					$63,659
Supplies (binders, Source Documents etc.)					$2,040
IRB Fee (IDC Excluded)					$3,500
Study Ancillaries/Per Subject Costs					
12-Lead ECG $250/Subject x 10 Subjects					$2,500
Research Pharmacy Dispense Study Drug 2/Subject $200 each x 10 Subjects					$4,000
Payment to Subjects $500 per Subject x 10 Subjects					$5,000
Total Non Personnel					$17,040
Total Direct Costs					$80,700
**** Indirect Costs @ 25% TDC**					$19,300
TOTAL COSTS					**$100,000**

Invoiceable – Pass Through

- Prescreening/Chart Reviews
- IRB Amendments/Cont. Review
- IND Safety Reports
- SAE Reporting
- Study Monitoring Visits
- Advertising/Recruitment
- Document Translation
- Research Pharmacy
- Study Closeout
- Record Storage

Commonly Missed Budget Items

- Not Accounting for Enough Staff Time
  - Investigator
  - Co-Investigator
  - Medical Staff
  - Nursing
  - Research Coordinator
  - Data Management

Remember: In Clinical Research, it always takes longer than you plan

Common Budget Mistakes

- Underestimating the time required for start-up
  - Site Initiation
  - IRB Approval Delay
- Overestimating the ease of recruiting subjects
  - Patient Population
  - Inclusion/Exclusion Criteria
- Under-budgeting for the unexpected
- Not including Invoiceables – Pass Thru Expenses
- Payment Terms

Commonly Missed Budget Items

- Missing IRB Fees (Initial; Amendments and Annual Reviews)
- Fringe Benefit & Institutional Indirect Costs (Verify rates with your institutional resource)
- Start-up Fee
  - Feasibility questionnaire; Site Initiation Visit; IRB prep
- Inadequate or no reimbursement for protocol procedures
- Annual cost increases for budget items
- Advertising Recruitment Costs
- Long Term Storage/Archive Fee
- F&A on Invoiceables

Consider "Hidden" Study Costs

- Delayed Study Start
- Delayed IRB Approval
- Lower than expected enrollment
- Supplies and expenses necessary for the study
  - Office Supplies
  - Photocopying charges
  - Phone/Computers
- Informed Consent Process
- Ancillary Cost Increases
- Research Pharmacy Drug Dispensing
- Shipping Supplies & Dry Ice
- Subject Stipend – Clin/Gift Card Activations Fee
- Central Lab vs. Local Lab
- Unscheduled Visits
- Query Resolution Time
- Increased salaries & operating costs over time
- AE & SAE Reporting
- Safety Reporting
- Screen Failures Time & Effort
- Study Monitoring – In Person or Remote
- Travel to clinics to offsite locations
  - Hotel stays
  - Tolls/Mileage
  - Meals
- Other Sponsor Requests

Developing Study Budgets

- Preparing Clinical Trial budgets is time-consuming and requires significant attention to detail. The time and effort invested upfront will ensure appropriate financial support for the life of the study.

"In clinical research, a site needs to anticipate that the time and effort necessary to successfully complete a study will be *significantly greater* than it would be to treat a similar number of regular-practice patients. It (the site) must negotiate a budget that provides adequate reimbursement for that extra time and effort"

The Investigator's Guide to Clinical Research

Dr. David Gisnberg, Centerwatch

Budget Negotiation

- Budget Process Requires Negotiation
- What is ideal versus bottom line?
- Compromise – Mutual Agreement

A well negotiated budget is making sure to include all costs of conducting the study

Payment Terms

- Another reason to prepare a budget prior to starting a clinical trial is that the budget, when done properly, should serve as a road map for invoicing.

Payment Terms

- Do you need to submit invoices to the sponsor for subject visits?
- Payments made monthly? Quarterly?
  - Payments are typically calculated based on completed eCRF's entered into a database (CTMS) maintained by the sponsor for work performed.
  - What prompts payment?
    - eCRF's
    - Study Monitoring Visit
    - Invoicing
  - Reminder to enter visit info into the EDC ASAP
    - Accurate information
    - Increases potential payment

Payment Terms

- Holdback
  - It is common for industry sponsors to hold back 10% of the per subject payment
  - What's your institutional policy?
    - Typically no more than 20%
  - Important to track for projection of final payment

Site Payments

- Request payments include your site investigator name and study name be entered in the check memo line.
- Request that the sponsor sends supporting documentation that itemizes the payment received.
    - Itemized details will help reconcile what was earned vs. what was paid

Who is Responsible for the Financial Management of Clinical Research Studies?

- Site Investigator
- The Research Administrator/Grant Administrator (all of us!)
- The Department Chair/Chief
- The Institution

Who is Responsible for the Financial Management of Clinical Research Studies?

Financial Management

- Review Finances Monthly
  - How much has been **earned**?
  - How much has the sponsor already **paid**?
  - How much has been **spent** on the fund?
  - How much does the sponsor **owe**?
  - How much is **remaining**?

- **If your site is not enrolling you are not getting paid**

Financial Management

- **Earned** $30,000 (3 Fully enrolled subjects)
- **Paid** $20,000 (Cash already received)
- **Spent** $25,000 (already charged to fund)
- **Owed** $10,000
- **Remaining** Balance $5,000

Financial Management

How much has been earned?

- Work with study team to get documentation of visits completed by subject
- Using the PSF Grid project future subject payments (or invoice) as well as invoiceables that can be invoiced to sponsor
- Monitor fund monthly
  - Increase/Decrease spending based on enrollment projections

In Conclusion

- Successful budgeting is essential to ensure all costs are covered
- No 2 studies are the same
- Budgeting is a challenge and time consuming part of the negotiation process and is necessary to ensure cost coverage
- Sites and sponsors need one another to successfully conduct clinical research
- Budgeting plays a large role in successful performance of clinical trials

Questions?

Thank you

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References

Essential Budgeting Requirements Associated with Conducting Clinical Trial Research

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Poster Presentation – Clinical Research Day 2010

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