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How to Prepare a Clinical Trial Budget

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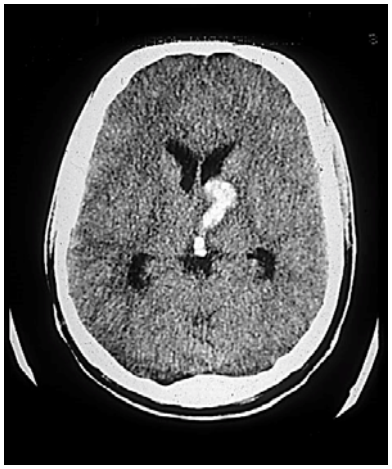
Definition of Trial Budget

- The estimated amount of money that you need to accomplish the goal of a clinical trial or study
- Study budgets are prepared overall and by each study year with costs linked to study tasks and patient recruitment.

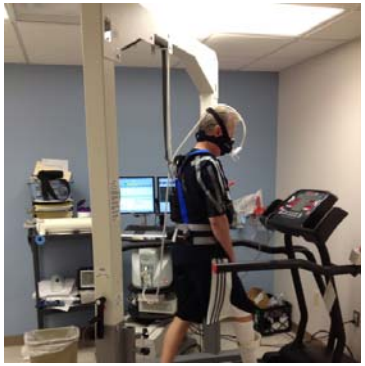
What are the Major Cost Buckets in a Budget

People who do trial work

Technology



Study-related care, including study intervention



Statistical Analysis and Data Management Support

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WebDCU™
Data → Information → Knowledge

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Travel and Meetings

Two Types of Trial Budgets: Overall and Site

- Overall – you are the PI of a multicenter or single center trial and are responsible for all parts of the budget (focus for today)
- Site budget – you are the local site PI and are negotiating with industry or other funding source regarding how much you get paid for start-up of trial/study, per patient enrollment, and study close-out.
  - In NIH StrokeNet, site budget is fixed, including overhead, and not negotiated at site level (already some support for PI and coordinator as part of RCC award.)
  - In industry trials, there is often some negotiation room in some but not all areas. Indirect rate is institutional specific.

Principle – Overall Budget Reflects Scope of Work

- You need to know.
  - **What is the clinical question to answer?**
  - **How many patients are needed to answer question?**
  - **How many sites are needed to recruit patients over what period of time?**
  - **What will be measured to determine safety and clinical outcomes?**
  - **What are the per patient costs in terms of technology (imaging, labs, etc.), treatments (drugs, devices), and personnel time to screen, enroll, measure outcomes, follow subjects, and data entry?**
  - **Who is running/coordinating the trial and what are their effort/costs/expenses?**
  - **Who providing statistical analysis and managing and monitoring data and what are their effort/costs/expenses?**
  - **What are the travel and communication costs to train trial staff and sites?**
  - **What additional costs of technologic measurements (image analysis, labs, etc.)are required?**
  - **Are you using consultants/advisors and how much do they cost?**

Principle: Every Task and Data Point Costs Money

- Less is more – minimizing data points makes trial easier and decreases budget. Carefully consider what is truly needed.
- Imaging is expensive – choose imaging that is part of standard of care (SOC) unless critical to clinical question that is being asked

Principle: Never underestimate Time and Sites to Recruit

- If you underestimate, you will greatly exceed budgeted infrastructure costs (coordinating center, trial leadership, data management/statistical support) which are usually based on FTE even though your per patient costs remain the same: e.g. 7 years to do planned 5 year study.
- If you need more sites later, won't have budgeted start-up costs for sites.
- NIH trial awards are now milestone-based and study will be stopped if recruitment doesn't meet targets

Principle: Pay for Time to Do a Task rather than FTE, If Possible

- Example: If you pay for 1.0 FTE coordinator and you recruit 2/3 of what you expect in 5 years, you will have no monies in subsequent years to pay for coordinator work if you are to complete trial and stay within budget
- Example: If you pay for 0.5 FTE for image analysis but have 2/3 the images expected after 5 years, you will have nothing left to pay for image analysis in subsequent years.
- Leadership of trial (e.g. PI(s), key personnel, study manager, data manager and statistical analysis) is generally in FTE

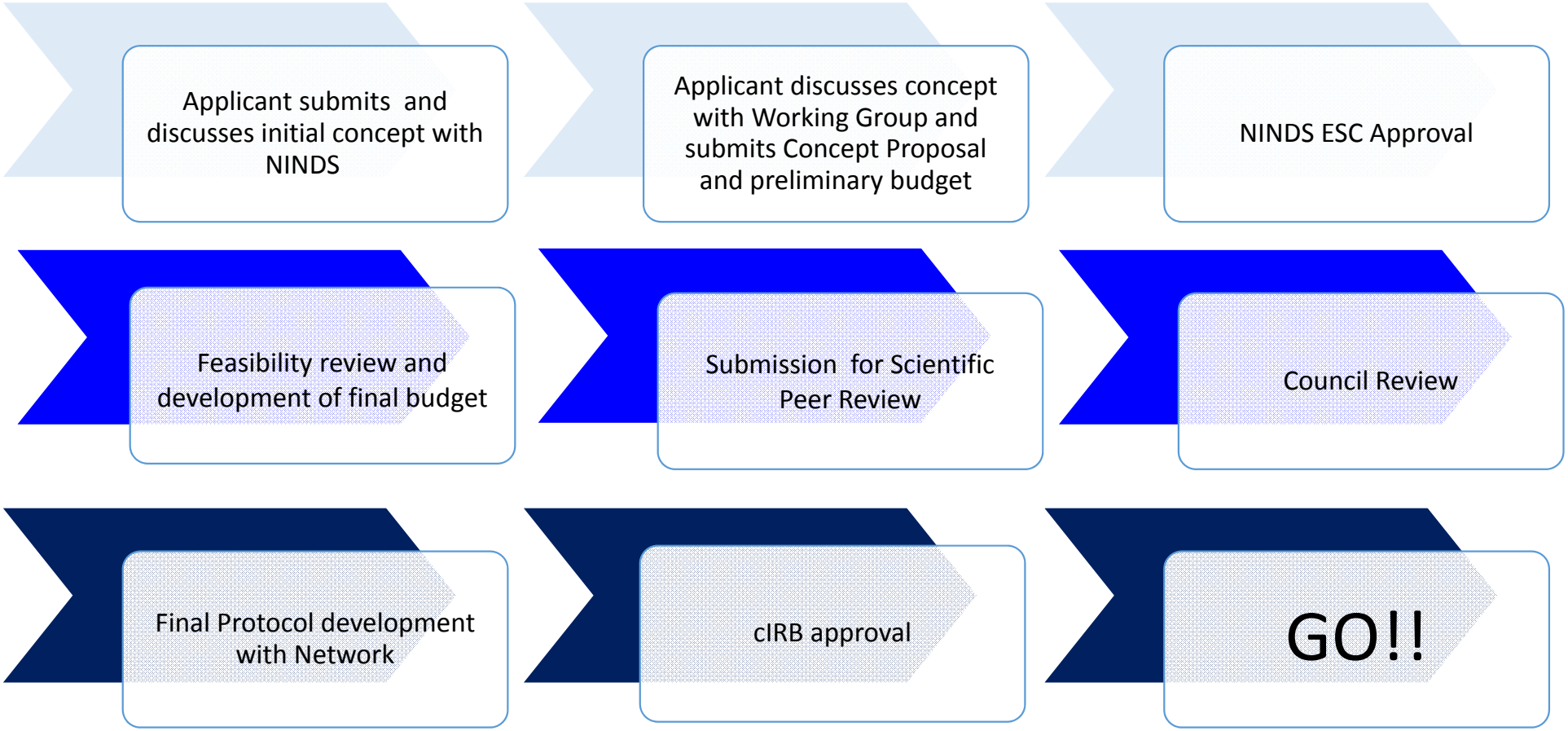
Principle: Talk to Experienced PIs, Coordinators

- Coordinators can give you good estimates of time for specific tasks. If you do overestimate time, do so with coordinator effort since they are the backbone of the site success.
- Experienced PIs can help with estimated effort estimates, per patient budget, and timing of different budgetary items.

Working with NIH

- < $500,000 in direct cost a year, don't need approval by NINDS to submit but always should talk to program officer.
- >$500,000 in direct cost a year, need prior NINDS approval to submit.
- For multi-center stroke trials, you will need to prepare a concept proposal and preliminary budget.
- Once concept proposal is deemed feasible and approved for submission, need to have final budget. It needs to be as accurate as possible since if you do need to resubmit, you can only have up to 10% budget increase.
- Maximum institutional salary that NIH can support on grant - $185,100. Greater salaries have to be cost-shared by institution.

StrokeNet Trial Development Process (simplified)



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Schedule of Events (SOE) Drives Per Patient Budget

Study Visits	Screening	Enrollment and Randomization	Baseline Visit	Visit 2	Visit 3	Final Visit
Informed Consent	X					
Medical History	X					
Physical Exam	X					
NIHSSS		X		X	X	X
Vital Signs		X		X	X	X
Laboratory assessment -Serum Chemistry /hematology	X					X
Study drug or device Administration			X			
Adverse events			X	X	X	X

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Determine Costs of Procedures and Personnel

- For Procedures - Pre-negotiated Federal Rate- SN used the Average National Medicare Rate in calculations
  - Need the CPT or Procedure code for each test determined to be research related

- For Study Personnel – need "effort" estimates by time (mins/hrs/ per visit) and typical personnel and their estimated salary/benefits (MD Investigator, clinical study coordinator (RN), non RN trial coordinator, MA's …) for each item on the SOE. Use upper range of salaries since west and east coast institutions have higher costs of living.

- Don't forget to include or consider budgeting time for subject screening activities, subject travel and parking, scheduling and phone contacts with subjects, the potential for unscheduled visits and data entry and site visits.

Need to Know What is Standard of Care vs. Research

- Consider not all Standard of Care (SOC) is national and therefore maybe locally or institutionally driven. What will be this trial's SOC items?
- Subjects or their "payers" should *never* be expected to bear the "cost" of research related procedures –CMS especially objects. If you pay for *some* procedures for *some* subjects Medicare feels you should pay for them *all*.
- How will sites address the potential subject that is uninsured.
- Does this trial meet the criteria for CMS reimbursement for SOC?

Example- Per subject Budget

Per subject reimbursement detail; n=1754							
Assessment	Performed by:	Baseline*	1 year f/u	2 year f/u	3 year f/u	4 year f/u	Total
Written Informed Consent:	PI	$ 75.00					$ 75.00
Inclusion/Exclusion Criteria:	PI	$ 75.00					$ 75.00
Randomization:	PI	$ 75.00					$ 75.00
Documentation of UIA (radiology, symptoms)	PI	$ 75.00					$ 75.00
Medical History/demographics/VS:	NC	$ 37.50					$ 37.50
Weight	NC	$ 12.00					$ 12.00
Height	NC	$ 12.00					$ 12.00
Physical exam	PI	$ 75.00	$ 75.00	$ 75.00	$ 75.00	$ 75.00	$ 375.00
Neuro exam	PI	$ 75.00	$ 75.00	$ 75.00	$ 75.00	$ 75.00	$ 375.00
Concomitant Medication Review	NC		$ 37.50	$ 37.50	$ 37.50	$ 37.50	$ 150.00
Adverse Event review	PI		$ 75.00	$ 75.00	$ 75.00	$ 75.00	$ 300.00
Questionnaires	NC		$ 75.00	$ 75.00	$ 75.00	$ 75.00	$ 300.00
MRA ($396) w/o GAD or CTSA ($422)		$ 422.00		$ 422.00		$ 422.00	$ 1,266.00
Serum myeloperoxidase blood draw	NC	$ 37.50		$ 37.50		$ 37.50	$ 112.50
Reporting events ($315k total from PPI) (~2.5 hrs)	NC	$ 183.57					$ 183.57
Sample shipping preparation	NC	$ 37.50		$ 37.50		$ 37.50	$ 112.50
Patient travel for follow up			$ 75.00	$ 75.00	$ 75.00	$ 75.00	$ 300.00
TOTAL DIRECT COSTS PER SUBJECT							$ 3,836.07
StrokeNet F&A on applicable elements							$ 1,490.40
TOTAL PER SUBJECT							$ 5,326.46

TOTAL SUBJECT REIMBURSEMENT BUDGET REQUEST	$ 9,342,616

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What are the IRB and Other Institutional Costs?

- The fixed and upfront costs…Traditionally covered or budgeted as **start-up fees**- and should not exceed $5000. per site max.
  - Include IRB or administrative fees
  - Pharmacy fees including close out and administration fees
  - Ancillary reviews (Radiology, clinical engineering, Nursing)
  - Institutional CMS analysis
- StrokeNet
  - Assumes IRB startup fee but needs to allow for institutional ancillary reviews etc…
  - Remember the “indirect” rate for SN is currently 42%.

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Placebos can be More Expensive than Study Drugs

- For budgeting you need the cost of active drug (or placebo) or device *by subject* not by dose *(e.g. – may need two vials for a big person)*
  - Kits are easiest to manage by most clinical performance sites
  - How many kits are needed per site and what is the cost per kit?
  - Consider waste or overage in final estimate. Remember, drugs can expire! Another reason why keeping to recruitment goal is important.

- Consider cost for meeting Standards for Investigational product (IP) -
  - Must consider the cost of demonstrating product stability for compounded agents and expiration of all study provided investigational product
  - Must consider additional cost of "blinded" packaging

- Shipping costs of IP –
  - Can it be shipped ambient and/or does it need temperature monitoring?
  - Is weight a factor?
  - How often does it need to be replaced (off the shelf) due to IP expiration or site use or waste?

StrokeNet additional costs

- NCC costs/fees
  - Central Pharmacy time
  - Program manager time
  - CIRB non StrokeNet sites
  - Reliance agreements and Protocol trial agreement time for NON network sites

- NDMC costs/fees
  - Statisticians (unblinded and/or blinded)
  - Data Manager
  - Programing for Database development
  - Data monitoring (maybe remote)

Overall NCC costs

StrokeNet NCC Costs	Total Protocol Costs	Network (70 sites)	Non-Network (10 sites)
Travel - NCC A[redacted] Proj Manager & NCC PI (or designate) to annual DSMB meetings and annual investigator meetings ($1,500 per trip)	42,000		
Site start-up payments ($2,000 per site)	160,000	140,000	20,000
Protocol Trial Agreement doc prep, non-network (10 non-network sites)	2,000		2,000
Document management, FFATA complince & reporting, non-network (10 non-network sites)	600		600
Master Trial Agreement TEMPLATE	115		115
Master Trial Agreement doc preparation, non-network (10 non-network sites)	3,200		3,200
Parent Protocol Approval (cIRB)	2,480	2,480	
Initiation Amendments for non-network child sites (10 non-network sites) (cIRB)	7,550		7,550
Approve Protocol Amendments (assume 1 per year) (cIRB) (10 non-network sites)	3,350		3,350
Approve Administrative Amendments (assumes 5 changes in staff or materials per site x 80 sites) (cIRB)	58,000	58,000	
Conduct Continuing Review (annual) (cIRB)	8,050		
Conduct Reportable Event Review (assume 2 over 7 years) (cIRB)	670	670	
Ongoing site communication (cIRB)	6,000	6,000	
Central Pharmacist effort, [redacted] 30% 7 years)	273,196		
Central Pharmacist Technician effort, TBD (100% 7 years)	465,859		
Project Management (1.0 FTE per year, 7 years)	864,674		
Labels (approximately 33,290 over course of study) (budget 34k)	1,258		
Pill bottles (~$1 per bottle, 33,290 needed) (budget 34k)	34,000		
Drug/placebo manufacture and stabilty testing (U of Iowa)	1,643,712		
Shipping expenses (2000 total shipments @ $35 assuming FedEx national average for Standard Overnight Delivery) (5 shipments per site per year x 80 sites x 5 years)	70,000		
TOTAL DIRECT COSTS, StrokeNet NCC Trial-Specific Support	3,646,714		
F&A (includes recovery on first $25K paid to non-network sites)	2,129,594		
TOTAL COSTS, StrokeNet NCC Trial-Specific Support	5,776,308		
PER PATIENT DOLLARS TO SITES (assuming n=1,754; n=877 subjects per arm)	9,342,616		
GRAND TOTAL, UNIV CINCINNATI StrokeNet NCC ARREST FUNDING REQUEST:	15,118,924		

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Final NCC Overall

Sponsoring Agency :	(NINDS prime)					**Titled :**		
Principal Investigator :	Broderick							
Period :	11/01/16	thru	10/31/23					
						Year 1		
A. ılaries						**Sal**	**FB**	**Total**
Senior Personnel	App't Type	% Effort	PM		Salary			
PI Broderick	ACAD	0.00%	0.00	$	-	-	$0	-
B. Other Personnel								
Exempt Staff (Monthly)	Name							
	TBD Proj Manager	100.00%	12.01	$	83,029	83,029	32,188	115,217
	[redacted]	30.00%	3.60	$	87,444	26,233	10,170	36,403
	Central Pharm Tech	100.00%	12.01	$	45,000	45,000	17,445	62,445
	Total Exempt Staff					154,262	59,803	214,065
	Sub Totals					154,262	59,803	214,065
Total Salaries and Fringe Benefits :						**214,065**		
E. Travel								
Domestic	Proj Mngr & NCC PI (or designate) DSMB and Investigator Mt					6,000		
International	(list)					-		
Total Travel :						**6,000**		
G. Supplies and Other Direct Costs								
Materials & Supplies	Labels & pill bottles for drug and placebo					-		
	Drug & Placebo manufacturing and stability testing (U Iowa)					-		
	Site start up payments ($2,000 per site, 80 sites)					160,000		
	Shipping (2000 total shipments @ $35 per shipment, FedEx standard overnight)					-		
	StrokeNet CIRB and Contracting Trial-Specific support					13,145		
	Per patient reimbursement to sites (no F&A recovery except for first $25k paid to					-		

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Final NCC Overall –pg2

4) F&A on first $25k paid to non network sites						-
Total Supplies and Other Direct Costs :						173,145
			TOTAL DIRECT COSTS:			**393,210**
			Facilities and Administrative Cost Base:			393,210
Facilities and Administrative Costs Calculation:						
F&A Cost (on MTDC):	58.00%	58.00%	58.00%	58.00%	58.00%	228,062
Sub-Contract <$25,000 1):	58.00%	58.00%	58.00%	58.00%	58.00%	0
Sub-Contract <$25,000 2):	58.00%	58.00%	58.00%	58.00%	58.00%	0
Sub-Contract <$25,000 3):	58.00%	58.00%	58.00%	58.00%	58.00%	0
Sub-Contract <$25,000 4):	58.00%	58.00%	58.00%	58.00%	58.00%	0
Total F&A Cost :						**228,062**
Total Cost						**621,272**

Facilities and Administrative Data

Purpose of Grant / Contract :	R	(R = Research, I = Instruction, P = Public Service, S = Special Rate on To
Special F&A Rate :	10.00%	
Campus Status :	C	(C = On Campus, O = Off Campus)

Detailed F&A figures for prorated rates	58.00%	152,041.33	58.00%
*If both lines have the same rate, then just list as one line on forms.	58.00%	76,020.67	58.00%
		228,062.00	

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Overall Pg3.

Grants / Contracts
5 Year Budget

Year 2			Year 3			Year 4			
Sal	FB	Total	Sal	FB	Total	Sal	FB	Total	Sal
-	$0	-	-	$0	-	-	$0	-	-
84,690	33,255	117,945	86,384	34,352	120,736	88,112	35,480	123,592	89,874
26,758	10,507	37,265	27,293	10,854	38,147	27,839	11,210	39,049	28,396
45,900	18,023	63,923	46,818	18,618	65,436	47,754	19,229	66,983	48,709
157,348	61,785	219,133	160,495	63,824	224,319	163,705	65,919	229,624	166,979
157,348	61,785	219,133	160,495	63,824	224,319	163,705	65,919	229,624	166,979
219,133			**224,319**			**229,624**			**235,051**
6,000			6,000			6,000			6,000
-			-			-			-
6,000			**6,000**			**6,000**			**6,000**
35,258			-			-			-
273,952			273,952			273,952			273,952
-			-			-			-
11,667			11,667			11,667			11,667
13,145			13,145			13,145			13,145
1,532,103			1,557,103			1,557,103			1,557,103

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Overall Pg. 4

Year 5		Year 6			Year 7			CUMULATIVE
FB	Total	Sal	FB	Total	Sal	FB	Total	
$0	-							-
								-
								-
36,639	126,513	91,671	37,374	129,045	93,504	38,122	131,626	864,674
11,576	39,972	28,964	11,809	40,773	29,543	12,045	41,588	273,196
19,857	68,566	48,709	19,859	68,568	49,683	20,256	69,939	465,859
68,072	235,051	169,344	69,042	238,386	172,730	70,422	243,152	1,603,730
								-
68,072	235,051	169,344	69,042	238,386	172,730	70,422	243,152	
		238,386			**243,152**			**1,603,730**
		6,000			6,000			42,000
		-			-			-
		6,000			**6,000**			**42,000**
		-			-			35,258
		273,952			273,952			1,643,712
		-			-			160,000
		11,667			11,667			70,000
		13,145			13,145			92,015
		1,557,103			1,557,103			9,317,616

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Site Monitoring is a **Big** Cost

- What is risk based monitoring?
  - Basing the actual source data verification (SDV) on ongoing data review or a planned review of a sampling or percentage of actual data (based on risk)
  - Can replace traditional 100% SDV

- How often will a monitor need to visit a site?
  - Minimum is once a year (monitor cost includes actual monitor salary, travel and expenses, report and paperwork generation time)

What to avoid---

- Enrollment Incentives
- Finders or referral fees
- Paperwork completion fees

- SN uses a per subject fixed fee approach.
  However, Allocation of funds for specific trial tasks /costs can be used at the sites discretion

Summary – How to Prepare a Budget

- Start early
- Talk to knowledgeable investigators and coordinators.
- Talk early to coordinating and data management centers
- Knowing the number of patients and number of sites needed to recruit them is fundamental
- Add technology only when critically needed
- Tend to overestimate than underestimate budget to accomplish goal but realize that sticker shock can leave a study undone.
- The study most likely to be approved by any organization is one which answers a critical question, has a straightforward, simple design, and has a reasonable and clear budget