SUNY RF
The Research Foundation for
The State University of New York
Downstate Medical Center

Fundamentals of Research Administration

Office of Research Administration
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Agenda – Industry Clinical Trials

- What is a Clinical Trial?
- The Contract – Pesky Terms and Conditions
- PI's Responsibility – What is it and What does it mean?
- Review and Preparation of the Budgets
- What does Pre-Award review? What is your sPA looking for?
- Internal Requirements – What's Necessary?
- The Signature Process

Definition of a Clinical Trial

- A prospective, biomedical or behavioral research study of human subjects
  - Designed to answer specific questions about biomedical or behavioral interventions (drugs, vaccines, biologics, treatments, medical devices) OR
  - Designed to test new ways of using known drugs, vaccines, biologics, treatments or medical devices
  - Behavioral interventions are intended to prevent or treat an acute or chronic disease or condition.

What is a Clinical Trial

- A research study used to determine whether new biomedical or behavioral interventions are safe, efficacious and effective.
- There are four phases of clinical trials and each phase is designed to answer a specific and separate research question

Clinical Trials – Phase I

- A study to test a new drug or treatment
- Small group of people for the first time
- Evaluate its safety;
- Determine a safe dosage range
- Identify side effects.

Clinical Trials – Phase II

- To test the drug or treatment in a larger group of people
- Determine if it is effective
- Further evaluate its safety

Clinical Trials – Phase III

- The drug or treatment is given to even larger groups of people
- Confirm its effectiveness
- Monitor side effects
- Compare it to commonly used treatments
- Collect information that will allow the drug or treatment to be used safely

Clinical Trials – Phase IV

- Studies performed after the drug or treatment has been marketed
- Gather information on the effect in various populations
- Determine what, if any, side effects are associated with long-term use

Who's Involved ?

- Office of Research Administration
  - Pre-Award Division
  - Post-Award Division
- Pharmacy
- Institutional Review Board
- Institutional Biosafety Committee
- Office of Technology and Commercialization
- The Hospital

ORA, Pre-Award Division

- Reviews, negotiates and executes Confidential Disclosure Agreements (CDAs) and Non-Disclosure Agreements (NDAs)
- Assists in the preparation of Investigational Device Exemptions (IDEs) and Investigational New Drug applications (INDs)
- Negotiates Clinical Trial Agreements (CTAs)
- Provides assistance and consultation with budget preparation
- Interacts and communicates with sponsors, clinical research organizations (CROs) and other entities

ORA, Post-Award Division

- Collects revenue based on the executed contract
- Prepares and processes invoices that do not require case report forms (CRFs)
- Works with the study coordinator to record and follow up on the receivables generated by CRFs

Other Offices

- Research Pharmacy
  - Stores and provides drug preparation for your clinical trials
  - Follows all sponsor and federal requirements in regards to dispensing and destroying medications
- Institutional Review Board
  - Responsible for reviewing and approving all IRB protocol submissions
- Institutional Biosafety Committee
  - Responsible for reviewing and approving all safety protocol submissions
- Office of Technology Transfer
  - Provides assistance as it relates to inventions, intellectual property rights and ownership

The Contract – Terms and Conditions

- Are…
  - requirements of every negotiation
  - “pesky” in nature
  - worth fighting for

Confidentiality Agreements

Confidentiality Agreements

- When is this required?
- Why is it necessary?
- Why does this need institutional signature?

Clinical Trial Agreements

Clinical Trial Agreements

- Publication Rights
- Confidentiality Terms
- CRF timelines, Investigator duties
- Intellectual Property
- Payment terms
- Indemnification, Liability, & Insurance
- Subject Injury & Biological Samples

Publication & Confidentiality

- Timeframes
- Review by Sponsors & editing
- What if there is no desire to publish?

Investigator Responsibilities

- CRF timelines
- Record retention
- Drug storage
- Representations on financial disclosure

Intellectual Property

- Who cares?
- Who wrote the Protocol?
  - Industry
  - Investigator
  - Hybrid

Indemnification & Liability

- Why does it matter?

Indemnification Example:

See page 3 of the handout

- CRO and Sponsor shall not be responsible for, and Institution and Investigator shall indemnify, defend and hold CRO and Sponsor harmless from any loss or third party claim resulting from (i) a failure to comply with the terms of the Protocol, or this Agreement or CRO and Sponsor's reasonable written instructions; (ii) failure to comply with any applicable rules and/or regulations; or (iii) the Institution, Investigator or Research Staff's negligence, willful misconduct, or their breach of this Agreement.

Subject Injury

- Why is it important?
- Scope and conditions
- Informed Consent issues

Subject Injury Example 1

See page 3 of the handout

- Pursuant to the informed consent document approved by SPONSOR and the IRB and signed by the Trial Subject ("ICF"), Research Organization will provide or arrange for treatment of a Trial Subject that is injured or becomes ill as a result of participation in the Trial. SPONSOR will reimburse Research Organization for medical expenses related to such treatment provided that:
  - The injury or illness for which medical treatment is provided was sustained as a direct result of the Investigational Product or any Trial procedure performed in accordance with the Protocol as mutually determined by SPONSOR and the Investigator; and
  - SPONSOR determines that the injury or illness is not associated with the Trial Subject's disease or condition or with the expected complications of the usual therapies for such disease or condition; and
  - If the injury or illness is the result of a procedure, the procedure was not one that the Trial Subject would have received but for participation in the Trial; and
  - The Trial Subject's failure to (i) follow the directions of Investigator, (ii) notify Investigator of the injury or illness as soon as possible following onset, or (iii) follow medical advice regarding the injury or illness did not cause or contribute to the injury or illness; and
  - The treatment provided was reasonable, customary and medically necessary to treat the injury or illness

Subject Injury Example 1

- Pursuant to the informed consent document approved by SPONSOR and the IRB and signed by the Trial Subject ("ICF"), Research Organization will provide or arrange for treatment of a Trial Subject that is injured or becomes ill as a result of participation in the Trial. SPONSOR will reimburse Research Organization for medical expenses related to such treatment provided that:
  - The injury or illness for which medical treatment is provided was sustained as a direct result of the Investigational Product or any Trial procedure performed in accordance with the Protocol as mutually determined by SPONSOR and the Investigator; and
  - SPONSOR determines that the injury or illness is not associated with the Trial Subject's disease or condition **or with the expected complications of the usual therapies for such disease or condition**; and
  - If the injury or illness is the result of a procedure, the procedure was not one that the Trial Subject would have received but for participation in the Trial; and
  - The Trial Subject's failure to (i) follow the directions of Investigator, (ii) notify Investigator of the injury or illness as soon as possible following onset, or (iii) follow medical advice regarding the injury or illness did not cause or contribute to the injury or illness; and
  - The treatment provided was reasonable, customary and medically necessary to treat the injury or illness

Subject Injury Example 2

See page 3 of the handout

- *Sponsor will reimburse Institution, at usual and customary rates, for the reasonable and necessary out-of-pocket medical expenses in excess of a Study Subject's commercial medical or hospital insurance, that are incurred by Institution for the acute medical care provided by Institution of adverse reactions directly resulting from use of the Study Drug in accordance with the Protocol; provided, that such adverse reactions or injuries are not attributable to (i) an Institution Indemnitee's negligence, willful misconduct or failure to adhere to the Protocol; or (ii) a pre-existing medical condition of the Study Subject, his/her underlying disease, or events that would have been expected from the standard treatment using currently approved therapies for the Study Subject's condition.*

Subject Injury Example 2

- *Sponsor will reimburse Institution, at usual and customary rates, for the reasonable and necessary out-of-pocket medical expenses in excess of a Study Subject's commercial medical or hospital insurance, that are incurred by Institution for the acute medical care provided by Institution of* ***adverse reactions*** *directly resulting from use of the Study Drug in accordance with the Protocol; provided, that such adverse reactions or injuries are not attributable to (i) an Institution Indemnitee's negligence, willful misconduct or failure to adhere to the Protocol; or (ii) a pre-existing medical condition of the Study Subject, his/her underlying disease,* ***or events that would have been expected from the standard treatment using currently approved therapies for the Study Subject's condition****.*

Biological Samples

- Why does it matter?
- Informed Consent Issues

Impact on the Informed Consent

- Subject Injury
- Use of Data
- Biological Samples

The Clinical Trial Budget …

- Needs to be somewhat flexible
- Must cover all costs
- Outlines what sponsor is required to pay for
- Fixed and Start-up Costs
- Costs related to subject visits

The Budget

- Patient Care Costs (i.e. ancillary tests)
- Study Supplies (i.e. blood collection tubes, binders, etc.)
- Subject Travel and Remuneration
- Subject Enrollment
- Travel

The Budget

- Shipping (i.e. biologics – blood, urine, tissue, saliva)
- Equipment or Proprietary Supplies (scales, software, instruments)
- Fees for Research Team

The Budget

- Study Drug
- Screen Failures
- Subject Injury / Adverse Events
- Start-up Costs

Additional Costs

- Publication Costs
- Retention of study records
- Advertising
- Professional Fees
- Institutional Costs

Internal Capitation Budget

see handout

DETAILED BUDGET FOR BUDGET PERIOD		FROM start date			THROUGH end date		GRANT NUMBER	
Personnel: STATE ""								
NAME	**Role**	**Hours Per Week**	**Inst. Base Salary**	**Weeks Per Study**	**Rate Per Visit**	**Salary Requested**	**Fringe Benefits**	**TOTALS**
Name	PD/PI				$0	$0	$0	$0
	Study Coordinator				$0	$0	$0	$0
	Res. Coordinator				$0	$0	$0	$0
	Recruitment Coordinator				$0	$0	$0	$0
	Res Coordinator				$0	$0	$0	$0
	Research Nurse				$0	$0	$0	$0
Total State Personnel		**0.00**		**0**		**$0**	**$0**	**$0**
Personnel: RES FDTN ""								
NAME	**Role**	**Hours Per Week**	**Inst. Base Salary**	**Weeks Per Study**	**Rate Per Visit**	**Salary Requested**	**Fringe Benefits**	**TOTALS**
Name	Study Coordinator				$0	$0	$ -	
	Research Nurse				$0	$0	$ -	
	Lab Technician				$0	$0	$ -	
	Postdoc				$0	$0	$ -	
	Graduate Student				$0	$0	$ -	
	Graduate Student				$0	$0	$ -	
	TBD				$0	$0	$ -	
Total RF Personnel		**0.00**		**0**		**$ -**	**$ -**	**$ -**
Equipment:	**Cost**	**Per**		**Units**				
								$ -
								$ -
Total Equipment								$ -
Supplies:	**Cost**	**Per**		**Units**				
Blood draw supplies								
Dry ice								$ -
Office supplies								
Disposables, i.e. needles								
Miscellaneous								
Total Supplies								$ -
Ancillary Tests: ""	**Cost**	**Per**		**Units**				
Blood draws, i.e. CBC								
MRI's								
X-rays								
Cat Scans								
Pet Scans								
HIV tests								
Laboratory costs - Hematology								$ -
Laboratory costs - Urinalysis								$ -
Pregnancy tests								$ -
Total Ancillary Tests								$ -
Travel:	**Cost**	**Per**		**Units**				
Airfare		person/trip						
Hotel		person/trip						
Meals		person/trip						

Internal Capitation Budget

Total Travel								$ -	
Subject Expenses: ""	**Cost**	**Per**		**Units**					
Subject travel		trip						$ -	Can be subway, cab or airfare for the subject ONLY. This can not be used for s
Outpatient food / meals		visit						$ -	" study specific for patients only; NOT parties, events, employee meals, etc
Subject reimbursement								$ -	remuneration for participating in the study
Total Subject Expenses								$ -	
Pharmacy Expenses: ""	**Cost**	**Per**		**Units**					provided by Research Pharmacy
Study Drug								0	
Pharmacy Prep Fee								0	
Dispensing									
otal Pharmacy Expenses								$ -	
Patient Care: ""	**Cost**	**Per**		**Units**					
Inpatient beds		patient						$ -	Does the hospital have a bed charge for overnight stays?
Outpatient beds		patient						$ -	
Total Patient Care								$ -	
SUBTOTAL per patient DIRECT COSTS FOR BUDGET PE								$ -	
				MODIFIED TOTAL DIRECT COSTS					for federal only (remove ancillary tests, remove equipment, pharmacy dispensing, binders & office supplies)
			FACILITIES AND ADMINISTRATIVE COSTS @				**25.0%**	$ -	25% for CT only; 61.5% research rate for everything else
TOTAL per patient COSTS FOR BUDGET PERIOD								$ 1	divide this number by the # of patients to get the per patient cost
									(unless you've only budgeted for 1 patient above)
INVOICEABLES: " These costs are variable and study specific. Please review your protocol and determine what you'll need from the sponsor. Study may not actually collect on the items below, work must have been performed and amount reflects maximum sponsor will pay. Most times it will be less, except for institutional									
INVOICEABLES: "	**Cost**	**Per**		**Units**					
Startup cost		1						$ -	typically request 1/2 of planned enrollment
IRB fee (initial)	3000	event		1				$ 3,000	set cost - industry sponsored studies: $3,000 initial review
IRB fee (substantiv	500	event		1				$ 500	set cost - industry sponsored studies: $500 for substantive review
IRB fee (continuing	1000	event		1				$ 1,000	set cost - industry sponsored studies: $1,000 for amendment
IRB fee (continuing	1500	event		1				$ 1,500	set cost - industry sponsored studies: $1500 amendment with substantive chan
Re-Consent Fee		subject		1				$ -	ask sponsor to cover costs if you're required to change protocol and re-consent
Translation Fee									translate consent form
Screening								$ -	
Screen Failures		event						$ -	
SAE's		event							
SC off-hour support		hour							will the Study Coordinator have to work off-hours (nights & weekends)
Pharmacy off-hour support		occurrence							will the Pharmacy have to work off-hours (nights & weekends)?
PI off-hour support		occurrence							will the PI have to work off-hours (nights & weekends)
Pharmacy Start-up	1500	1						$ 1,500	provided by Research Pharmacy
Pharmacy Close-ou	500	1						$ 500	provided by Research Pharmacy
Pharmacy Dispensing									provided by Research Pharmacy
Adjudication Package		package							if sponsor requires them
Advertising									
Record Retention/Storage									to be paid at study closeout
Lease / Rent space									is this being done off site?
"File technical reports									does sponsor require these?
"Training / Assessments								$ -	does anyone on the study team need to be trained? i.e. Research Nurse, etc
SUBTOTAL ADDITIONAL INVOICEABLES								$ 8,000	
					FACILITIES & ADMIN COSTS		25%	$ 2,000.00	25% for CT only; 61.5% research rate for everything else
TOTAL INVOICEABLES								$ 10,000	

Internal Study Budget

- Are any tests Standard of Care (SOC)?
- Is sponsor providing any supplies?
- Is sponsor paying for shipping of biologics?
- Is the study inpatient or outpatient?
- Is this a device trial? A drug trial?

Internal Study Budget

- Are other academic departments involved?
  - Radiology ?
  - Pathology?
- Calculating Effort
- Pharmacy Fees
- IRB Fees

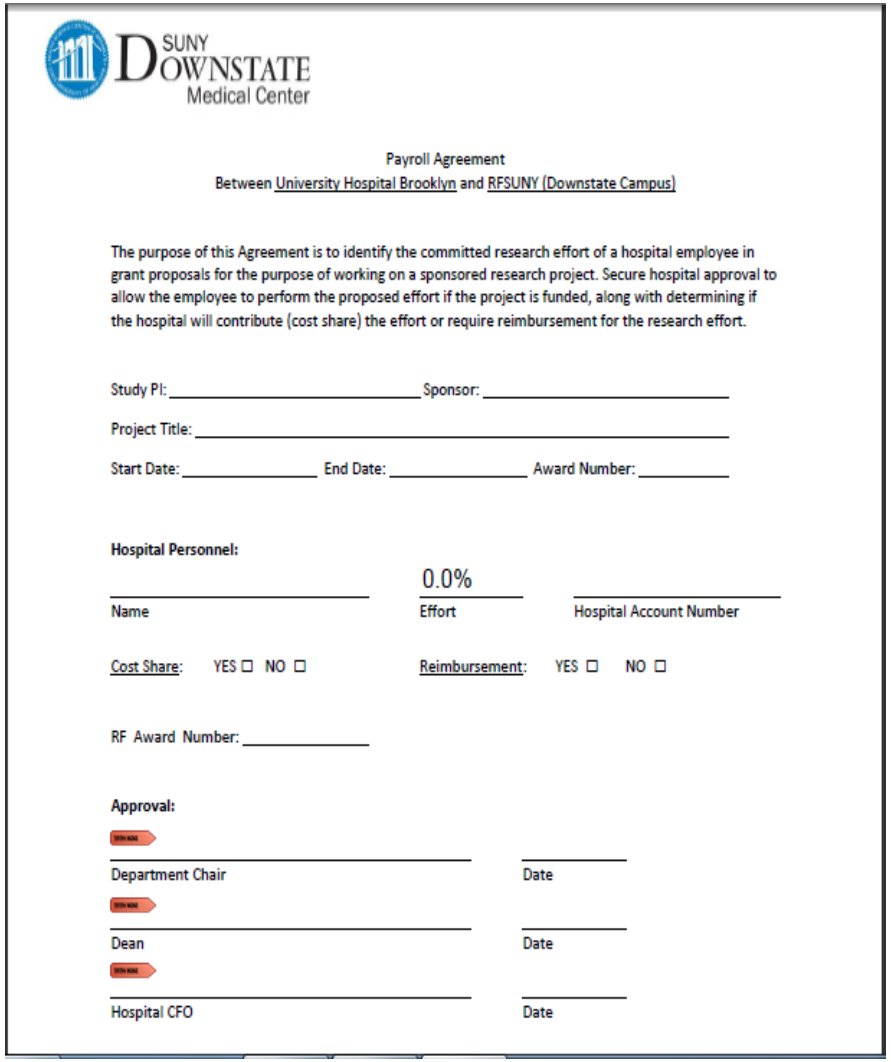
Pre-Award review

- Sponsored Project Associate (sPA)
  - Budget
    - Ancillary costs
    - Study Team effort
    - Professional Fees
    - Institutional costs

Cost-Share and the Hospital signature process

- Applicable when the cost-share is for a Hospital employee or when hospital resources are being used
  - Award number starts with a “3”
  - Award number is provided by the Department
- The Hospital CFO will sign in addition to the Dean and Department Chair
- All RF and Downstate policies remain the same

Hospital Cost-Share Form



SUNY DOWNSTATE Medical Center

Payroll Agreement
Between University Hospital Brooklyn and RFSUNY (Downstate Campus)

The purpose of this Agreement is to identify the committed research effort of a hospital employee in grant proposals for the purpose of working on a sponsored research project. Secure hospital approval to allow the employee to perform the proposed effort if the project is funded, along with determining if the hospital will contribute (cost share) the effort or require reimbursement for the research effort.

Study PI: _____ Sponsor: _____

Project Title: _____

Start Date: _____ End Date: _____ Award Number: _____

Hospital Personnel:

_____ 0.0% _____
Name Effort Hospital Account Number

Cost Share: YES ☐ NO ☐ Reimbursement: YES ☐ NO ☐

RF Award Number: _____

Approval:

_____ _____
Department Chair Date

_____ _____
Dean Date

_____ _____
Hospital CFO Date

Pre-Award review

- Contract Manager
  - The Agreement
    - Contract terms and conditions
    - Negotiation
    - Final execution of the contract

Finalizing of Agreements

- Who signs and when?
- What does “Read and Understood” really mean?

Institutional Requirements

- IRB approval
- Biosafety approval
- COI-SMART
- Routing paperwork
  - Proposal Tracking / Signature Worksheet
  - Cost Share Template

Requirements for Account Setup

- Budget and Contract are finalized
- Annual and Transactional questionnaires are complete
- Institutional paperwork is approved and signed
- IRB & Biosafety approval is in place

Account Setup for Clinical Trials

- We will upload the budget into Oracle, our financial system, in stages, depending upon the terms and conditions of the contract
- PI's responsibility not to exceed contractual amount
  - Fixed price contract, the budget for the fixed price will be uploaded
  - Milestone driven contract : An initial budget will be established for 20% PLUS any invoiceable items (IRB, startup, pharmacy, etc.) The initial 20% will be deducted from the final scheduled payments
  - Capitation contracts or per patient: An initial budget will be established for 20% PLUS any invoiceable items (IRB, startup, pharmacy, etc.) The initial budget of 20% will be deducted from the final per patient payments

CT updates for 2017

Clinical Trials – new policies for 2017

Clinical Trials – new Federal policy

- New DHHS regulation and NIH policy will be in effect as of **January 18, 2017**
- This will affect all NIH-funded clinical trials
- Initiatives aim to increase the availability of information to the public about clinical trials – information that is not systematically available from other public sources
- The Food and Drug Administration Amendments Act (FDAAA) expands ClinicalTrials.gov and imposes new requirements that apply to certain trials supported by NIH funds

FDAAA and Clinical Trials supported by NIH

- Trials subject to FDAAA are called "Applicable Clinical Trials" (ACT) and must be in full compliance with FDAAA
- Applicable Clinical Trials include:
  - *Trials of Drugs and Biologics*: Controlled, clinical investigations, other than Phase 1 investigations, of a product subject to FDA regulation
  - *Trials of Devices*: Controlled trials with health outcomes, other than small feasibility studies, and pediatric post market surveillance

The Final Rule…

- Applies to the Responsible Party for Applicable Clinical Trials (ACTs)
  - The Responsible Party is the sponsor of a CT or a designated PI
  - An Applicable Clinical Trial must meet 1 or more of the following criteria:
    - The CT must include one or more sites in the United States
    - Must study a drug, biological, or device product that is manufactured in the United States or its territories
    - Is exported for use in CTs outside the United States OR must
    - Be conducted under an FDA investigational new drug application (IND) or investigational device exemption (IDE)

The Final Rule requires …

- A responsible party:
  - must register an Applicable Clinical Trial in ClinicalTrials.gov no later than 21 days after enrolling the first participant
  - must submit summary results information to ClinicalTrials.gov regardless of whether the drug, biological, or device products under study have been approved, licensed, or cleared for marketing by the FDA
  - must submit summary results no later than 1 year after the primary completion date of the clinical trial

The Final Rule … and NIH

- The final NIH Policy complements the Final Rule in that the NIH Policy applies to ALL clinical trials funded in whole or in part by NIH, regardless of the study phase, the type of intervention, or whether the clinical trial is subject to the Final Rule
  - Includes Phase 1 trials of drug and biological products, small feasibility studies of device products, and clinical trials of behavioral, surgical, and other types of health and medical interventions

Compliance to the Final Rule

- A responsible party has 90 days (3 months) after January 18, 2017 to come into compliance – no later than April 18, 2017
- NIH is required to make a responsible party's non-compliance public through a posting on the clinical trial record
- The FDA has the authority to issue a Notice of Noncompliance to a responsible party who has failed to comply
- A responsible party who commits a prohibited act(s) may be the subject of an injunction action or criminal prosecution brought by the Department of Justice
- Compliance with the NIH policy will be via the terms and conditions of the NIH award

FDA Investigator Training in November 2016

- FDA is offering a FREE, 3-day training session
  - The training course is for clinical investigators, such as clinicians, nurses, pharmacists and other health care providers involved in conducting clinical trials
  - Intended to provide investigators with the expertise in the design, conduct and analysis of clinical trials, and to enhance the safety of trial participants
    - Course runs from November 7-9: must register https://www.federalregister/gov/d/2016-22348