How to Plan and Conduct a Clinical Trial

Division of Research & Economic Development

Lunch & Learn

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Office of Clinical Research:
Sue Breno CCRC

Office of Sponsored Programs:
Cathy Harlan MPA GPC CRA

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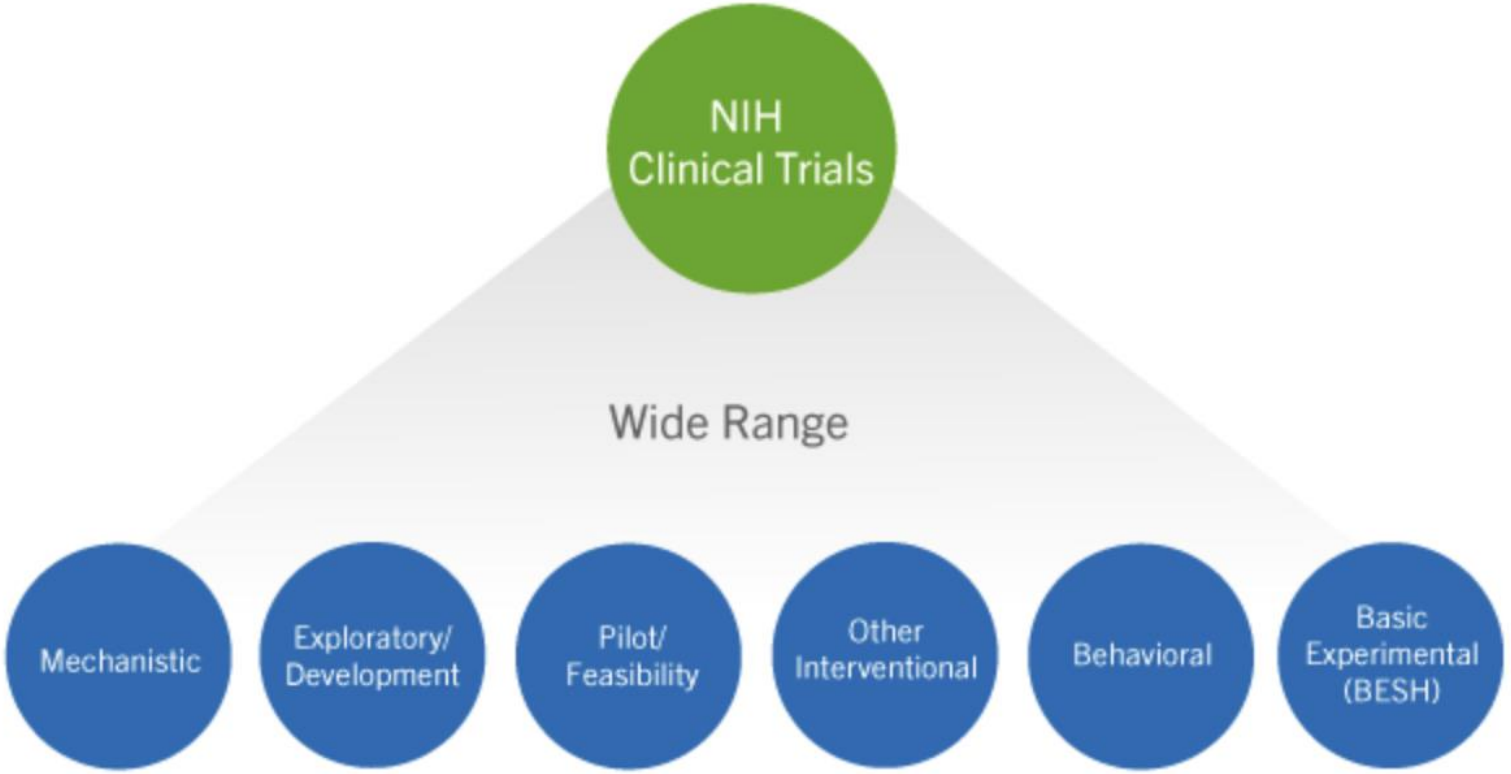
Today's Objectives

- Clinical Trials vs other types of Human Subject Research
- How Clinical Trials are supported at NSU
- What to do when considering conducting a human subject clinical trial
- What steps are required to open and conduct a clinical trial
- OCR services to guide and assist you through the study approval requirements

WHAT IS A CLINICAL TRIAL?

A clinical trial is defined as a research study in which one or more human subjects are **prospective**ly assigned to one or more **intervention**s (which may include placebo or other control) to evaluate the effects of those interventions *(or diagnostics)* on **health**-related biomedical or behavioral **outcome**s.



https://grants.nih.gov/policy/clinical-trials/definition.htm

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Human Subjects Research

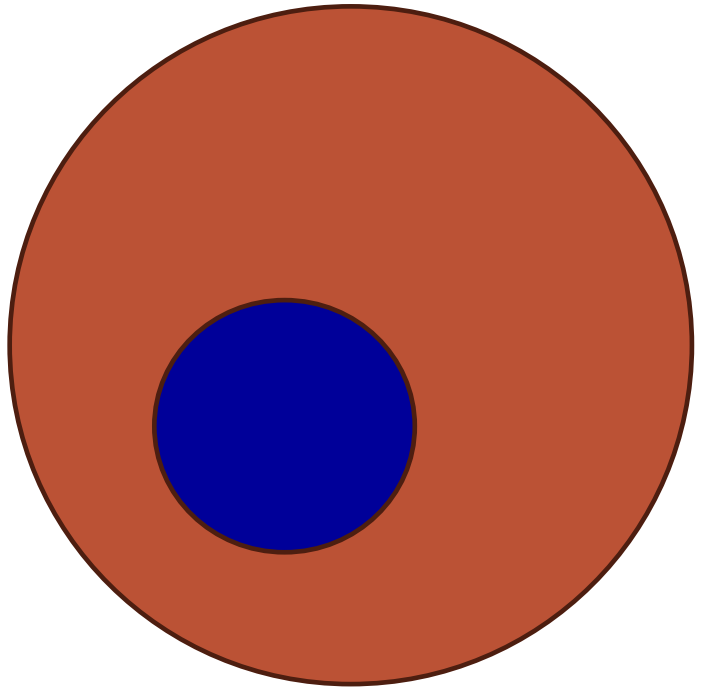
"Research involving a living individual about whom data or biospecimens are obtained / used / studied / analyzed through interaction / intervention, or identifiable private information is used / studied / analyzed / generated."

Examples of human subjects research include:

- Collecting blood
- Conducting a survey
- Changing participants' environment
- Administering medicine
- Interviewing
- Administering a psychological test
- Collecting data
- Conducting a focus group
- Testing a new educational technique

"These interventions include drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and diagnostic strategies."

https://grants.nih.gov/policy/humansubjects/research.html



Clinical Trials are a subset of **Human Subjects Research**

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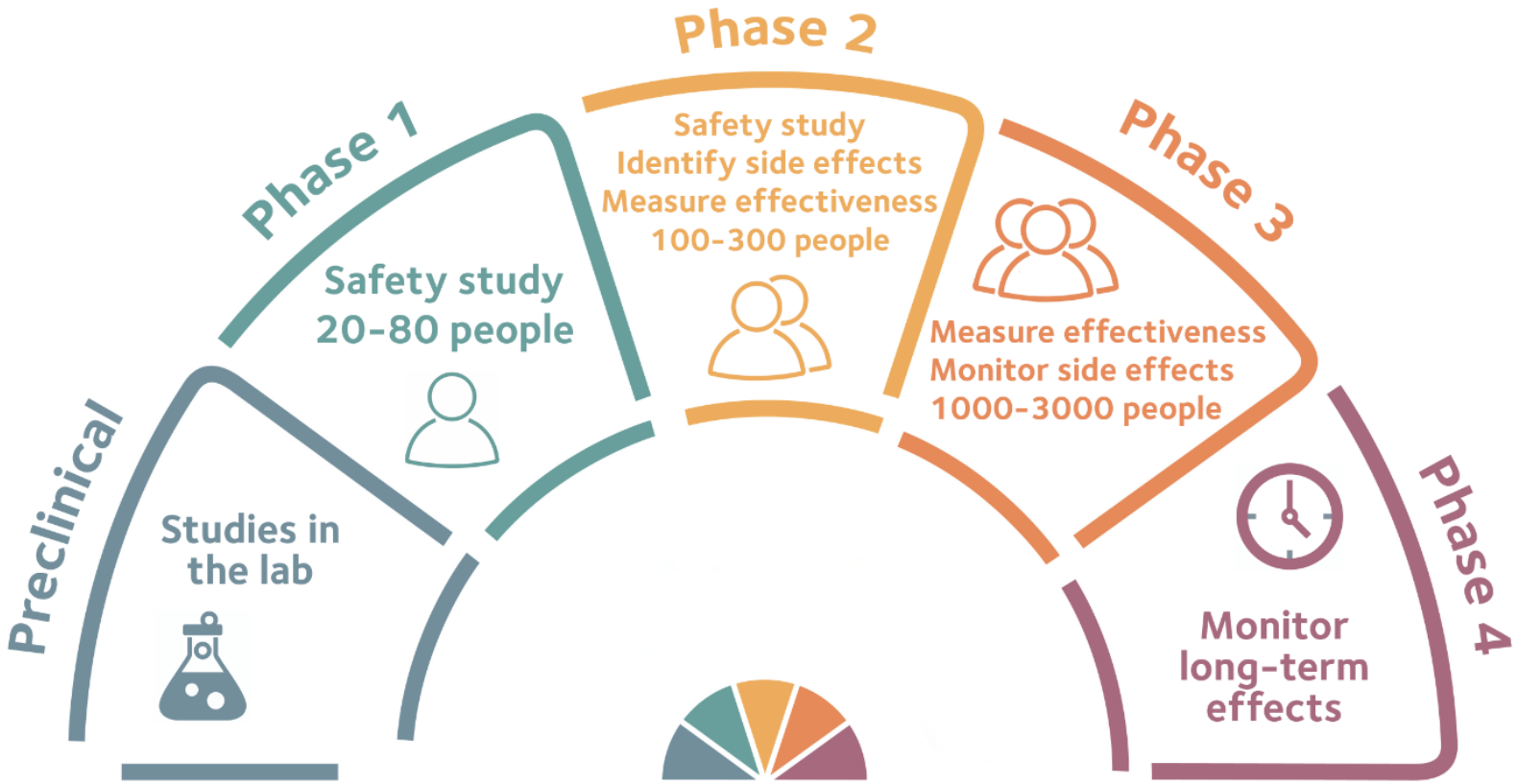
Stages of Clinical Trials



Pre- Clinical Studies

- Lab projects
- Observational or cohort studies

Pilot Study

- Feasibility of human testing

Phase 1

- Safety “first in human”

Phase 2

- Efficacy signal
- Side effects in larger study

Phase 3

- Compare to standard of care

Phase 4

- “post-approval” evaluation

https://tv.ndph.ox.ac.uk/clinical-trials/

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Types of Clinical Trials

- **Intervention:** Drug, Device, Behavioral, Procedure
- **Whose Idea It Was:** Investigator-Initiated, Industry-developed
- **Who is Responsible for Trial:** Investigator-Sponsor vs Industry-Sponsor
- **Funding Source:** department/college, university, external non-profit or for-profit

Lifecycle of a Clinical Trial

https://www.hopkinsmedicine.org/all-childrens-hospital/academics/research/clinical-research-lifecycle

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The Three "R"s of Research at NSU

Resources

Requirements

Research

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Resources

College Resources

Dean
Associate Dean for Research
College IRB Representative
College Business Representative
College HR Representative
Colleagues

University Resources

Division of Research
Institutional Review Board
Research Pharmacy
HPD Statistical Core
Core Research Facilities
INIM CLIA Lab

Resources

Division of Research and Economic Development

Office of Sponsored Programs

Supports **non-profit funded**
- NIH, DOD
- State and county agencies
- Non-profit organizations
- HPD, President's

Cathy Harlan
OSP@nova.edu

Office of Clinical Research

Supports **industry funded**
- Trials
- Informed Consent and HIPAA Authorization review
- Data use agreements
- ClinicalTrials.gov resource

Susan Breno
OCR@nova.edu

Grant Writing Lab

Supports **concept development for faculty and staff**
- Finding opportunities
- Grant applications
- Grantsmanship trainings

Melanie Bauer
GrantLab@nova.edu

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Resources

Office of Sponsored Programs

Cathy Harlan
Executive Director, OSP
OSP@nova.edu

PRE-AWARD

- Finding funding opportunities
- Assisting with budget development
- Developing subcontracts
- Checking application requirements
- Completing university approvals / assurances
- Submitting (for several funding systems)

POST-AWARD

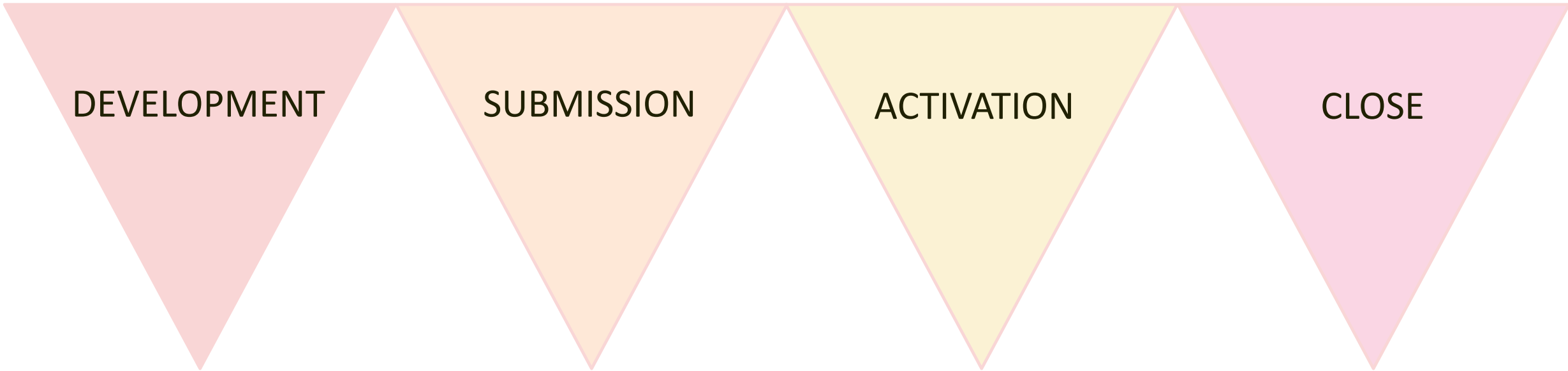
- Processing contracts and subcontracts
- Award administration
- Ensuring compliance with sponsor rules
- Assisting with annual and final reports and continuation applications

Resources

Office of Clinical Research

Susan Breno
Manager, OCR
OCR@nova.edu

Supports **industry funded trials**
both investigator or industry initiated



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Requirements

Pre-Award

Sponsor contacts PI or PI contacts External Funding Agency

Execute Confidential Disclosure Agreement

HOW? Contact OCR and include OCR in Industry communications

Until CDA signed, parties share limited information about the study

Requirements

Pre-Award

Sponsor contacts PI or PI contacts External Funding Agency

→ Execute Confidential Disclosure Agreement

→ Review Concept and/or Protocol, Budget

- Is there interest and feasibility?

For PI to consider: ability to enroll
scientific interest
competing studies active at NSU
sufficient monetary support

What Makes A Protocol?

"Trial protocols are documents that **describe the objectives, design, methodology, statistical considerations** and aspects related to the organization of clinical trials. Trial protocols provide the **background and rationale** for conducting a study, highlighting specific research questions that are addressed, and taking into consideration ethical issues. Trial protocols must meet a standard that adheres to the principles of Good Clinical Practice, and are used to obtain ethics approval by local Ethics Committees or Institutional Review Boards."

Research Protocol Template v 20240325

Instructions:
Black font is required for all studies, *italicized blue font is optional depending on type of study.*

1. Title Page (Version Date)
    a. Title
    b. Date / Version #
    c. College Association/Unit
    d. PI and other key personnel – contact info and roles
    e. *Funding source - if any*
        i. *Contracted Services*
        ii. *Subawards*
    f. Site
        i. On Campus Location
        ii. Off-Campus Location
        iii. Online
2. *Protocol Summary*
    Brief description. (Similar to Abstract on grant.gov submission)
3. Background / Aims
    a. Purpose Statement
    b. Objectives +/- Hypotheses
    c. *Impact*
4. Study Design (including Basic Timeline)
    a. Methodology
    b. Schedule of Events
    c. List of Data Collection instruments
5. Eligibility / Participant Population
    a. If Retrospective:
        i. How participants are identified
        ii. Selection Criteria
    b. If Prospective:
        i. Inclusion/Exclusion criteria (ie eligibility)
        ii. Screening (ie finding patients)
        iii. Recruitment (ie presenting study)
        iv. *Randomization*
6. Consent Process/Waiver of Consent, HIPAA Authorization

****Find TEMPLATE here: https://www.nova.edu/irb/manual/forms/index.html**

Cipriani A, Barbui C. What is a clinical trial protocol? Epidemiol Psichiatr Soc. 2010 Apr-Jun;19(2):116-7. PMID: 20815294.

**email IRB or OCR if template not posted yet

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Key Components to a Budget	
Length of Study	Number of Subjects and Anticipated Enrollment Period Follow-Up Length
Institutional Overhead	Federal: 54%; Industry: 30%; Employee Fringe 25.75%*
Study Personnel	Calculating Effort: hours per subject AND hours per administrative activity
One Time Study Costs	Startup, annual, and close out activities Pharmacy, Lab, external admin fees Capital Equipment Presentation/Publication costs
Schedule of Events	What Happens at Each Visit and does study or insurance pay for that activity
Itemized Costs per Subject	For study activities, what will it cost to complete visit? Include testing, subject reimbursement/compensation

*for NSU as of 4/3/2024

Key Components to a Budget

Length of Study	Number of Subjects and Anticipated Enrollment Period Follow-Up Length
Institutic	25.75%*
Study Pe	e activity
One Tim	
Schedule	
Itemized Costs per Subject	For study activities, what will it cost to complete visit? Include testing, subject reimbursement/compensation

Work with College Business Representative

Recommend using OCR template budget which will create

1) Funding Agency Budget

2) Schedule of Events

3) a Banner Index budget

4) Benchmark Revenue and Expense Guidance

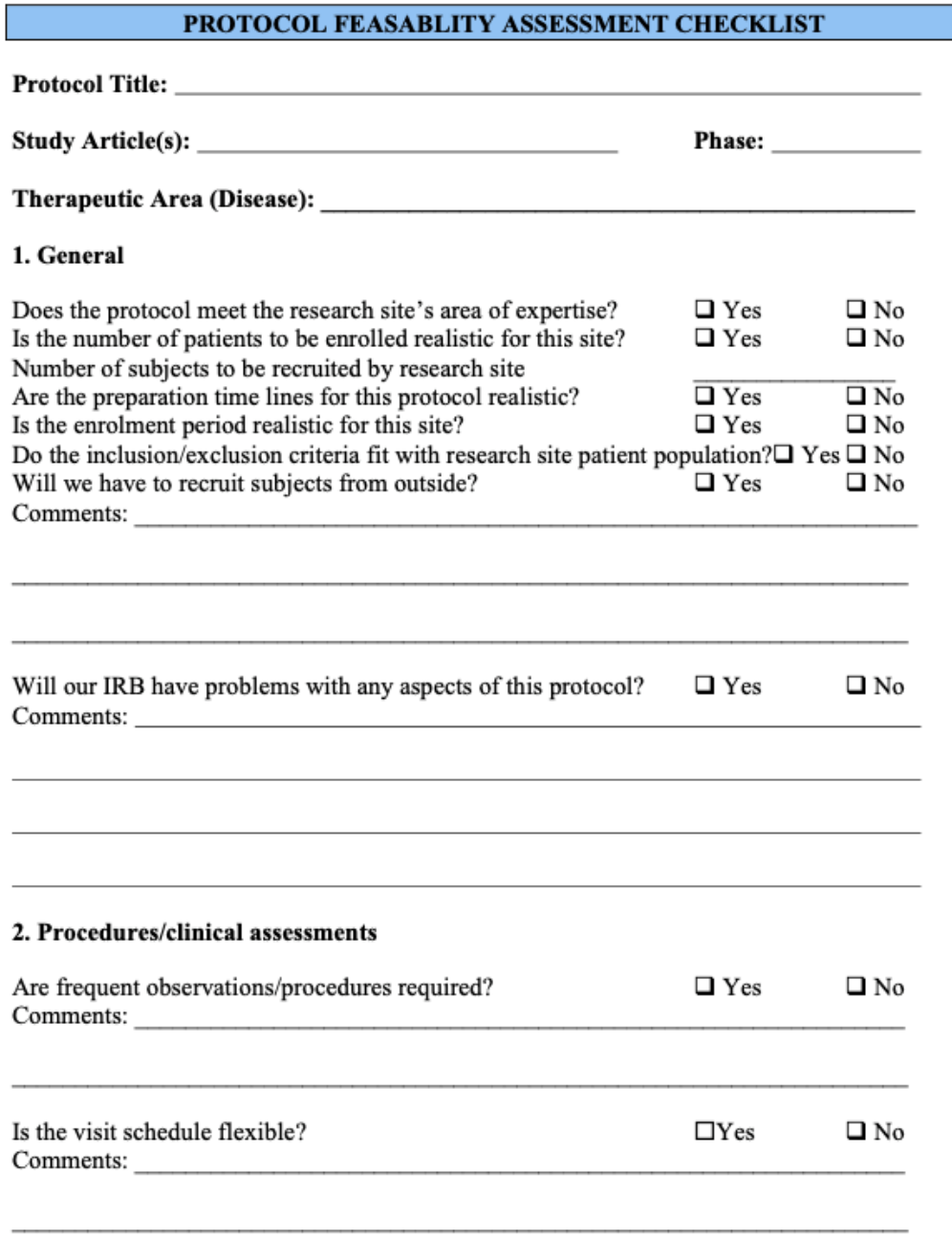
****IMPORTANT to budget every cost and study activity – common mistake is to underbudget**

*for NSU as of 4/3/2024 **Request Budget Consult HERE: https://www.nova.edu/ocr/starting-points.html**

FEASIBILITY CHECKLIST

OPTIONAL form to guide decision-making around feasibility of a study

- Enrollment Goal and Time Frame?
- Access to Suitable Subjects?
- Challenges to recruitment manageable?
- Any logistical challenges?
- How is data to be collected and shared?
- Adequate support?
- Any Research Ethics and Compliance issues?



PROTOCOL FEASABLITY ASSESSMENT CHECKLIST

Protocol Title: _____

Study Article(s): _____ **Phase:** _____

Therapeutic Area (Disease): _____

1. General

Does the protocol meet the research site's area of expertise? ❑ Yes ❑ No
Is the number of patients to be enrolled realistic for this site? ❑ Yes ❑ No
Number of subjects to be recruited by research site _____
Are the preparation time lines for this protocol realistic? ❑ Yes ❑ No
Is the enrolment period realistic for this site? ❑ Yes ❑ No
Do the inclusion/exclusion criteria fit with research site patient population? ❑ Yes ❑ No
Will we have to recruit subjects from outside? ❑ Yes ❑ No
Comments: _____

Will our IRB have problems with any aspects of this protocol? ❑ Yes ❑ No
Comments: _____

2. Procedures/clinical assessments

Are frequent observations/procedures required? ❑ Yes ❑ No
Comments: _____

Is the visit schedule flexible? ❑Yes ❑ No
Comments: _____

Find Feasibility Checklist here: https://www.nova.edu/ocr/starting-points.html

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Requirements

Pre-Award

Sponsor contacts PI or PI contacts External Funding Agency

→ Execute Confidential Disclosure Agreement

→ Review Concept and/or Protocol, Budget

- Is there interest and feasibility?

Sponsor: may schedule a Site Qualification Visit
or may ask site to complete questionnaire
to confirm expertise, resources, sufficient
eligible population

Requirements

Pre-Award

Sponsor contacts PI or PI contacts External Funding Agency

Execute Confidential Disclosure Agreement

Review Concept and/or Protocol, Budget

Get Approval for Resources

- People, Space, Funding

Protocol Approval Record

1) Must be completed by PI and signed by Dean
2) Includes key questions:
   - Type of award (contract or sub-contract) and contact info
   - Personnel effort requirements
   - Anticipated funding
   - Required NSU space and/or equipment
   - Possible conflicts of interest
3) Must be received by OCR to continue process

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NOVA SOUTHEASTERN UNIVERSITY

Nova Southeastern University
Office of Clinical Research
3300 S. University Drive
Fort Lauderdale, FL, 33328-2004

Protocol Approval Record

For Non-Federally Funded Human Subject Research

INSTRUCTIONS

1. Complete Section I to determine whether this form is required.
2. **Complete this form prior to Clinical Trial Agreement negotiations.**
3. The Principal Investigator (PI) is responsible for the completion of this form, including **obtaining all personnel and Deans' signatures**.
4. Once completed, this form must be electronically forwarded to the Office of Clinical Research ocr@nova.edu

Section I – Research Classification Questions

1. Is this a clinical trial? ☐ No ☐ Phase I ☐ Phase II ☐ Phase III ☐ Phase IV

   The NIH defines a clinical trial as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes (http://grants.nih.gov/grants/glossary.htm) .

2. If it is not a clinical trial, please describe the type of study below.

   _____

3. Has this study already been registered on Clinicaltrials.gov?

   ☐ No ☐ Yes, NCT# _____

SECTION II – Protocol

PI: _____

College / Center / Department _____

Phone ext. _____ Email_____ Cell phone _____

Protocol Title: _____

Proposed Start Date: _____ End Date: _____ Duration: _____Year(s) / _____Month(s)

Instrument of Award: ☐ Contract ☐ Sub-Contract

External Sponsor: _____

Address:

Find PAR here: https://www.nova.edu/ocr/starting-points.html

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Requirements

Pre-Award

- Sponsor contacts PI or PI contacts External Funding Agency
- Execute Confidential Disclosure Agreement
- Review Concept and/or Protocol, Budget
- Get Approval for Resources
- Execute Legal Agreements

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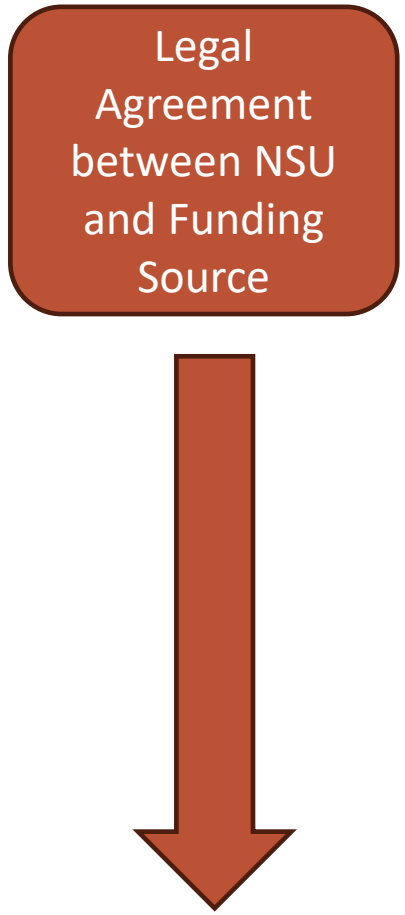
Clinical Trial Agreement

- Agrees to responsibilities of each Party regarding execution of study
- Negotiated by DoR and Funding Source
  - Katherine Rose, JD LLM AVP/Attorney
- PIs cannot sign for NSU – must be DOR
- Must include finalized budget, protocol, informed consent form
- Other Legal Agreements: Sub-contract, Ancillary Site, Material Transfer, Data Use Agreements



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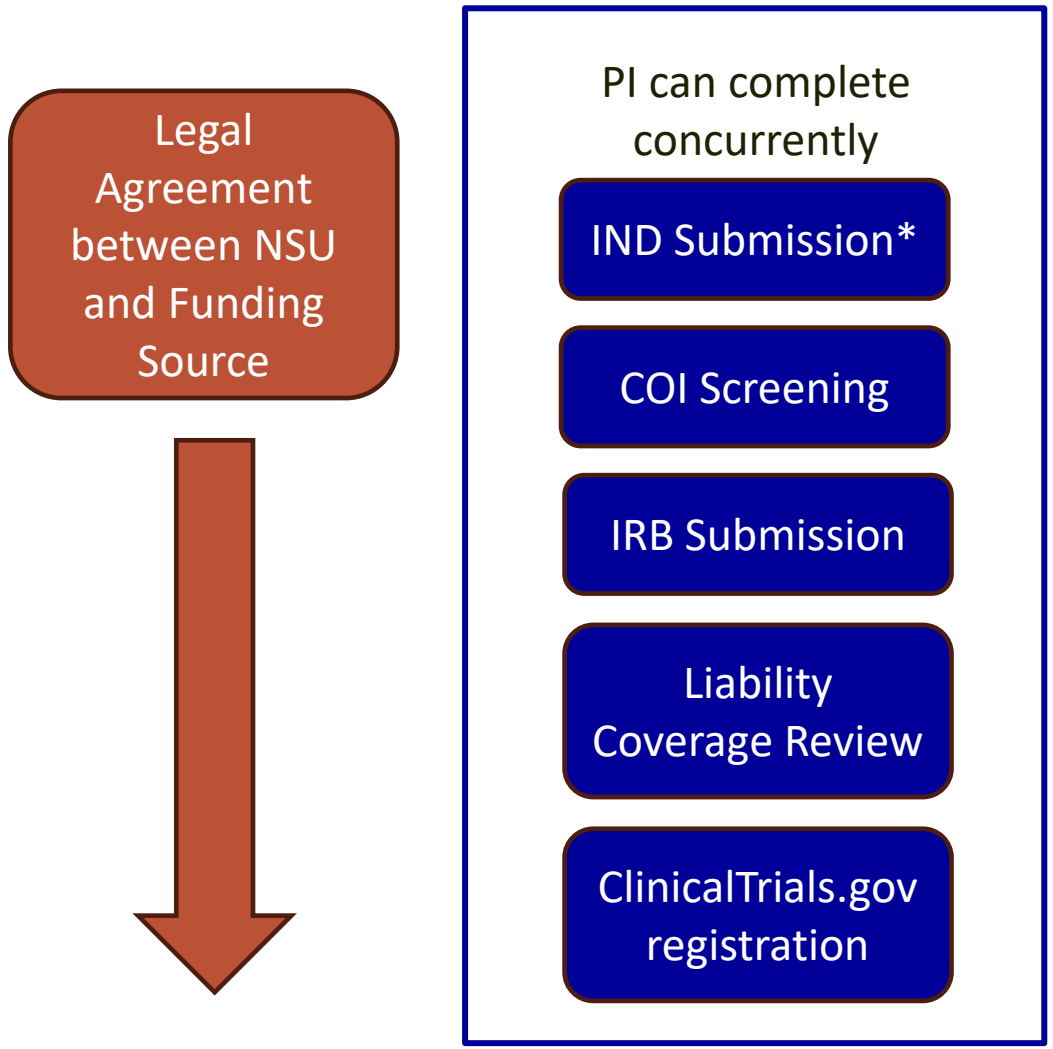

*IND submission IF Investigator is also Sponsor

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Is an IND or IDE Required? Whose Responsibility?

Sometimes Investigational New Drug / Investigational Device Exemption is required

An IND / IDE application is a request to the FDA for authorization to use an investigational drug/device in human studies. The investigational product can be pre-approval or for a different indication than already approved.

Typically whomever conceives of and designs trial will be sponsor and hold IND / IDE

IND and IDE discussions need DOR consultation

NSU Institutional Review Board (IRB)

https://www.nova.edu/irb

IRB approval is mandated prior to the initiation of any human subjects study activity.

**Chart reviews for potential subjects requires a Review Preparatory to Research approval

IRB reviews and approves:

- Initial Research Protocol
- Amendments (including any personnel changes)
- Annual Continuing Reviews
- Closing Report
- SAE Reporting
- Subject Instructions
- Recruitment Materials

Other necessary forms: HIPAA Authorization for Research

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) is a federal law that required the creation of national standards to protect sensitive patient health information from being disclosed without the patient's consent or knowledge.

Submitting to the IRB

- Electronic Submission system: https://www.nova.edu/irb/irbmanager/index.html
- You will need:
  - Protocol, ICF, Delegation Log, Training Documentation
  - Any Participant facing communications (Recruitment materials count!)

Training:

- Free and available on CITI (https://www.nova.edu/irb/training.html)
- NSU HIPAA Privacy Training (https://www.nova.edu/hipaa-privacy/training/course.html)

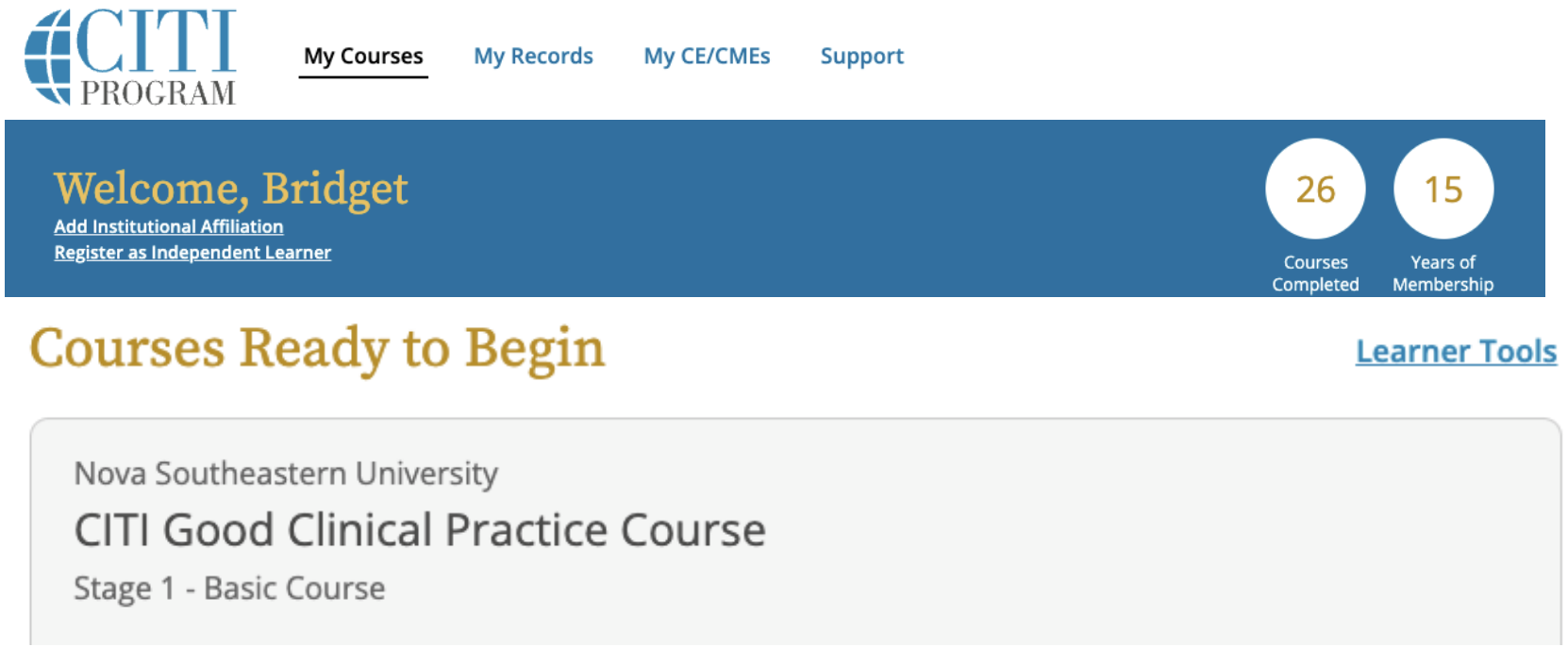
NSU Required Training for Clinical Trials

Through CITI:

- Required: Human Subjects Research (either “group 1: Biomedical (HPD) Researchers” or Group 2: Social-Behavioral-Educational (Non-HPD) Researchers”
- CITI Good Clinical Practice Course (for PIs and certain personnel)*

Through NSU:

- NSU HIPAA Training
- request through Privacy Office Luann Healy LHealy@nova.edu



*See policy OCR-2 here: https://www.nova.edu/ocr/policies-for-gcp/administrative-policies.html

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Liability Coverage Review

To document that compensation to subject(s) for trial-related injury will be available

OCR will submit protocol synopsis to NSU's insurance carrier

Protects all parties involved

REGISTERING ON CLINICALTRIALS.GOV

ClinicalTrials.gov is a databank or registry of federally funded, privately supported, and unfunded clinical trials involving human subjects.

… is the result of a federal law requiring that clinical trials be registered to improve public access to information about clinical research, promote public trust in research and inform future research. Medical journals also require prospective registration of trials to be considered for publications.

NSU requires that ANY clinical trial in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control or diagnostics) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.*

→ Request a ClinicalTrials.gov User ID from OCR

***See policy OCR-1 here: https://www.nova.edu/ocr/policies-for-gcp/administrative-policies.html**

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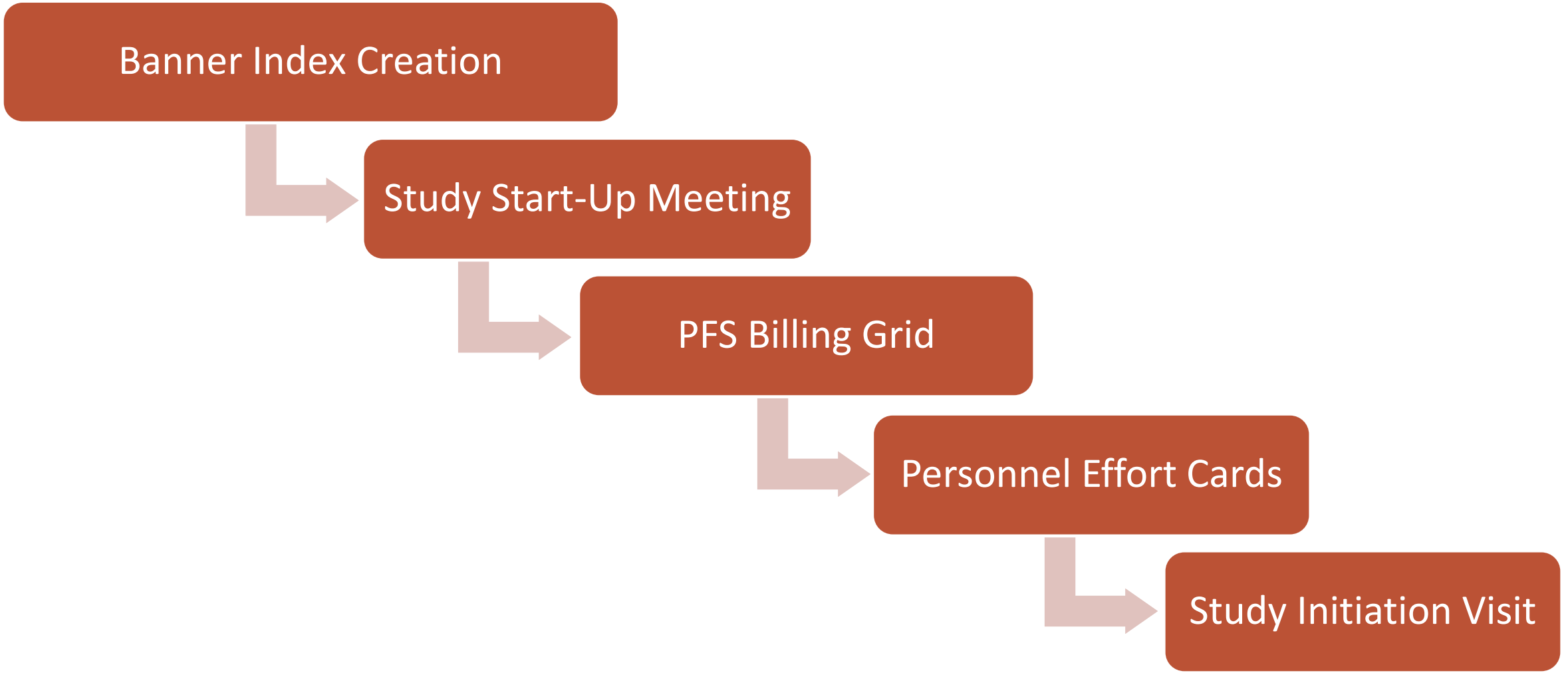
CONGRATULATIONS!!

Responsibilities of PI:

- is responsible for the safe and ethical conduct of the study and the quality and accuracy of the data
- ensures the study is performed according to the protocol and all applicable regulations
- is responsible for the safety of subjects enrolled on the study and for reporting of any safety events per protocol and regulations
- conducts, directs, or supervises research involving human participants to make certain that the research is consistent with NSU policies and procedures, and that the appropriate IRB has been informed of existing knowledge of any risks involved.
- report real or potential conflicts of interests with the annual COI survey and at any time a new COI relationship is made.

Requirements

Activation Process



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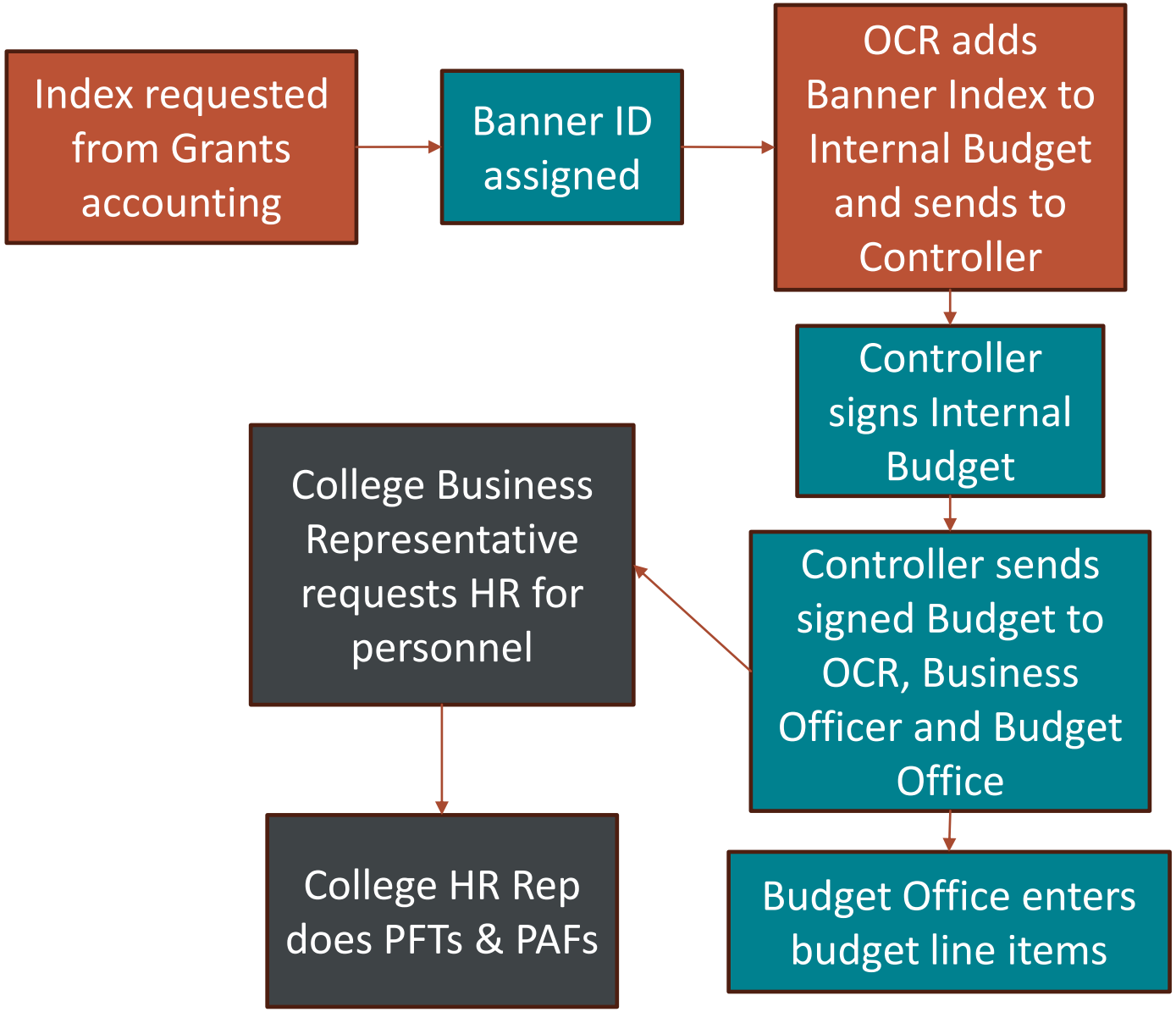
Setting Up a Research Account in Banner

OSP or OCR must send in request including:

1) Finance "New Account Request"
2) Project Summary "Digest"
3) Executed CTA
4) IRB approval
5) Approved Budget in Banner format
6) List of Approved Personnel for Index Access
   (PIs: work with OCR/OSP to create this list)



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Requirements

Activation Process

Banner Index Creation

Study Start-Up Meeting (NOT the SAME as SIV)

Regulatory Requirements:

- Regulatory Binder
- Accountability and Processes for Investigational Agents
- ClinicalTrials.gov – must be registered within 21 days of first subject; requires updates annually or with status change

Key People to include in Study Start-Up: Contracts & Grants Accounting Accountant assigned
College Business and HR Representatives
Pharmacy and/or Lab Leadership
NSU Health Billing Manager (Patient Financial Services)

Requirements

Activation Process

- Banner Index Creation
- Study Start-Up Meeting
- PFS Billing Grid*

*Required if any Standard of Care billing potential

In Schedule of Events, PI **must** itemize which activities are billed to research and which are billed to insurance/patient

CRITICAL COMPLIANCE STEP TO PREVENT FRAUD

HOW: Contact Patient Financial Services

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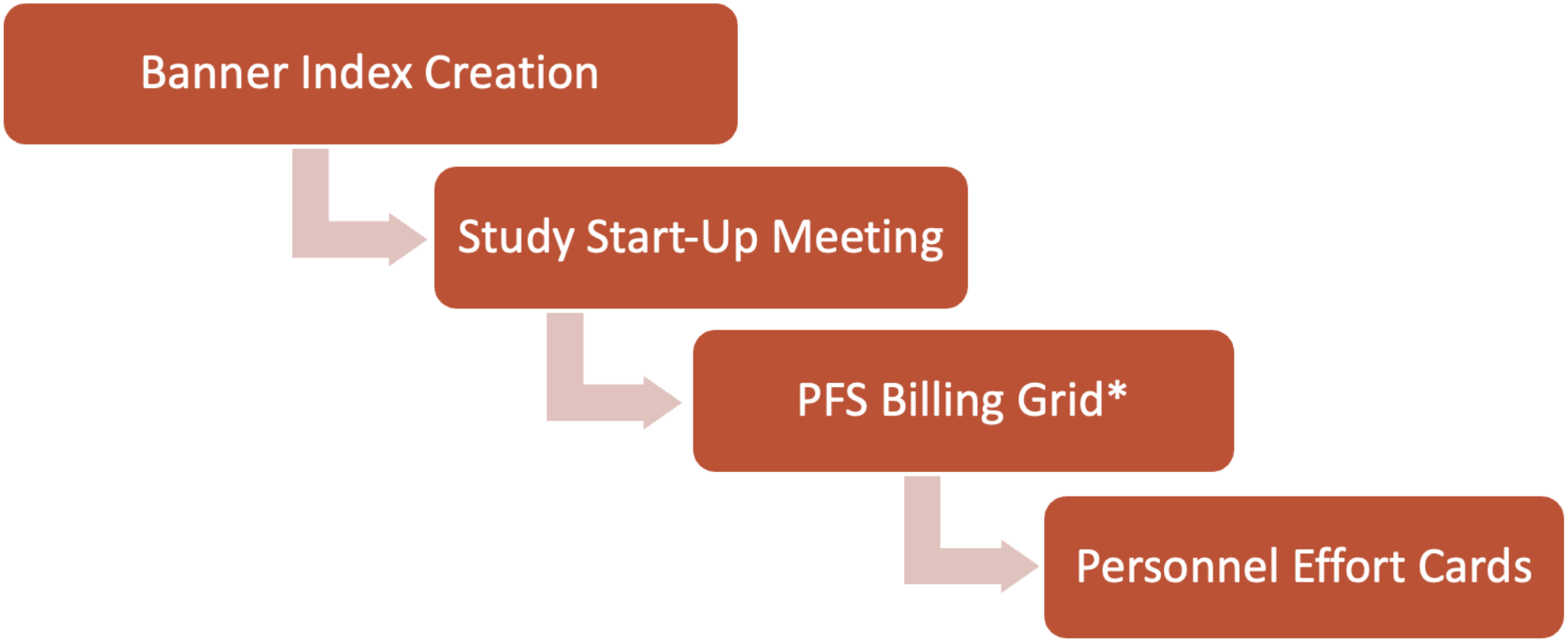
Requirements

Activation Process



Effort needs to match contract

eCert tracks all effort billed directly on research-tagged Indexes

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Requirements

Activation Process

- Banner Index Creation
- Study Start-Up Meeting
- PFS Billing Grid*
- Personnel Effort Cards
- Study Initiation Visit

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Research

Open Trial

- Enroll and Perform Study Activities
- Regular Financial Reconciliation
- Be Prepared for Audits
- File IRB Amendments and Annual Reports
- Study Close-Out

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Compliance with Regulatory Requirements for Study Conduct

Filing of all IRB communications

Adverse Event reporting

Protocol Deviations reporting

PI review of IND Safety reports (external sites)

- MedWatch reports

Data Safety Monitoring Board

Financial Conflict of Interest Updates

Infectious Substances Packaging and Shipping Training

Investigational Drug/Device Accountability

Biosafety - the prevention of large-scale loss of biological integrity

- Back up power in case of loss of electricity

Research

Open Trial

- Enroll and Perform Study Activities
- Regular Financial Reconciliation
  - Meet with CGA accountant and College Business Representative to review Index, Invoices, Revenue, and Expenses
- Be Prepared for Audits
  - Create a Regulatory Binder with all trial documentation
- File IRB Amendments and Annual Reports
- Study Close-Out

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Study Close-Out

When ALL study activities are complete and ALL revenue received

- Submit all data to Sponsor
- Correct any final Sponsor generated queries
- Review Regulatory Binder
  - missing documents
  - current credentials are filed
- Close IRB
- Update ClinicalTrials.gov
- Reconcile and close Banner Index

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Data Management and Storage

Sponsor will have requirements for maintenance of onsite access to study records after study closure. In absence of other guidance, NSU policy is to retain documents onsite for three years.

The longest most distant date shall be used as the destruction date. Per 21CFR312.62 An investigator shall retain records required to be maintained under this part for a period of 2 years 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 if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified OR its relevant successor or equivalent for non-drug studies OR the timeframe specified by the sponsor contractually, whichever is longer.

→ When ready to archive in long term storage, contact:

NSU Records Management https://www.nova.edu/records/index.html

Questions?

Division of Research: 954-262-7509
OCR@nova.edu