THE OHIO STATE UNIVERSITY

CLINICAL AND TRANSLATIONAL SCIENCE INSTITUTE

INVESTIGATOR INITIATED TRIAL GUIDEBOOK

V1: 3/20/2025

What is an Investigator Initiated Trial?

An Investigator Initiated trial (IIT) is a clinical trial in which the investigator conceives the research, develops the protocol and now may also serve as the sponsor. All research requires a sponsor and an investigator. The sponsor is the individual, company, institution or organization that takes on **legal responsibility** for the initiation, management and/or financing of the research (ICHE6(R2):1.53). IITs are often developed by PIs in academic medical centers. Many times, an IIT is lead and managed by the initiating PI instead of the groups that funds it (biotechnology company or government agency). IITs drive translational research by taking the information learned in the lab or clinic and applies that insight to real world practice.

Investigators many times develop an IIT trial without the realization of the full scope of sponsor responsibilities. Thus, they are woefully underprepared for the project management burden that exists and the **team** (Appendix A) that exists for industry studies and is helpful and many times necessary to have in place to ensure all parts of the study management are moving seamlessly to ensure the project comes to fruition, without delay and within compliance of federal regulations and guidelines. These project management tasks are far more in-depth than those a typical study coordinator would undertake for an industry sponsored research study.

As an IIT Principal Investigator, your job as the sponsor and investigator is to ensure that people have the information and training to properly conduct the research uniformly across all locations. A large or multi-center IIT should have budgeted effort assigned for a **project manager** at your site. This role is essential in the oversight of administrative tasks and documents for the study (Appendix B). If you do not have the support staff to administratively manage your project that does not mean you cannot do the project. You can subcontract with experienced academic Coordination/Data Centers or Contract Research Organizations. The CTSI network capacity team can help initiate that relationship.

For multi-centered (three or more locations) clinical trials, the **Trial Innovation Network** can assist with the planning and or implementation of your proposal https://trialinnovationnetwork.org/ . This service is free of charge and many investigators state it is like a pre-grant review committee to help you get a different perspective on your proposal by some of the nations most experienced trialists. You can apply for this service at an early stage in your proposal development or later as a pre-grant review ensuring you have considered all aspects prior to grant submission. They also have services you can purchase for trial management like a CIRB, project management team or data management team. You must apply with at least a 30-day window prior to grant submission to allow for adequate review by the team.

This guide serves as a basic project planning and management roadmap. This guidebook serves as a tool-kit to ensure investigators have thought about the many areas essential to help their trial grow from a simple idea to a funded grant.

Additional Resource:

1. Konwar M, Bose D, Gogtay NJ, Thatte UM. Investigator-initiated studies: Challenges and solutions. *Perspect Clin Res*. 2018;9(4):179-183. doi:10.4103/picr.PICR_106_18. PMID: 30319949

1. GETTING STARTED- YOUR BIG IDEA

☐ Write a rough proposal and determine specific aims and outcome measurements

- If you want assistance from the CTSI. Create a project under MyCTSI.
- Then develop a three-to-five page clinical study concept synopsis- include a summary of background, aims, outcomes and importance of study to provide to those you will be discussing the trial (Ohio State CTSI Intake Form).

☐ Complete literature review to see what studies have already been completed on this topic

- How did they complete their trials what tests/measures were used?
- Obstacles on past trials or improvements to be made in your proposal?
- Who funded their research? Might be an option for your submission as well.
  - https://reporter.nih.gov/ is a good resource to see what other NIH-sponsored studies are currently listed that may not published yet.
  - https://clinicaltrials.gov is another searchable resource for studies in planning, ongoing, or completed. This may include studies by a variety of sponsors.

☐ Discuss your proposal with a **Statistician – THIS STEP IS ESSENTIAL**

They will help develop your study design for your outcome measures and calculate your study sample size. The Clinical and Translational Science Award (CTSA) has a relationship with Bio-Medical Informatics with the Biostatistics, Epidemiology and Research Design (BERD) group if you do not have resources or funding within your department and need assistance with a new trial design.

https://go.osu.edu/rightquestion

☐ Assess the feasibility of the trial

- Supplies, staffing, locations of research, resources (administrative and clinical) participant access
- Do you have a study coordinator or project manager already on staff to manage the administrative components of your idea
- Can you meet your sample size goal at Ohio State, or do you need to recruit participants outside of The Ohio State University Wexner Medical Center and liaison with the public or with other institutions/centers?

☐ Funding Source

You must identify some funding to implement a successful IIT

- NIH funding can be searched https://grants.nih.gov/funding/searchguide/index.html#/
- Ohio State compiled a list https://erik.osu.edu/knowledge-enterprise-home/oke-funding
- Other government agencies (e.g., CDC) may fund a study, especially if associated with an emerging public health issue.
- Non-profit advocacy groups can supplement your proposal
- Pharmaceutical and smaller biotechnology companies may be willing to
  - fund studies
  - provide investigational products
  - provide database mechanisms (if they think the study may accentuate their label)

TIP: When an external entity is providing study product (drugs, devices, other materials), confer with the ERIK-Office of Innovation and Economic Development to ensure you have legal agreements in place for this exchange. These may be in the form of a materials transfer agreement or a contract.

TIP: Reach out to funding groups in the very beginning to make sure they are interested in your idea and if they have any restrictions on funding.

2. DEVELOPMENT/DESIGN COMMITTEE

☐ Create a Steering Committee that will help with the development and design of your proposal/protocol Your committee should include the following individuals to help mold and formulate your proposal for grant submission: Meet regularly with the **core group** and add in the specialty team members as needed. Your grant will be better formulated when created by a team.

Core Group

- **Two Mentors** or Investigators experienced in clinical research. They do not necessarily need expertise in your study. It is more important that they have developed protocols and been funded in the past.
- **Clinical research project managers/coordinators*** trial logistics
- **Statistician***

Specialty Team Members may include:

- Fiscal team member to aid in budget development*
- Advocacy Group Representative/ Patient Representative*.
    - The CTSI has community members who are trained and willing to assist in research.
    - Use someone from an advocacy group if your disease/condition has one. Having them engaged in the creation of the trial gets them more excited to champion the study within their organization's membership once it gets funded.
- Regulatory Team Member (IRB, compliance and bioethics)*
- Specialist in outcome measures (if applicable) (ie...MRI- radiology, muscle testing- physical therapist, infusion center- have a nurse from the potential dosing location).
- Pharmacist (if drug involved)
- Clinical Lab manager (if specimens are to be collected)

***Represents tasks the CTSI can assist if you do not have an identified study team member**

Tasks to be Determined by the Design/Development Committee

- Inclusion/Exclusion Criteria
- Study length
- Number of visits and location (can some be remote?)
- Tests to be completed at each visit (schedule of events-this helps steer your budget)
- Staffing for study (Staff List or a Delegation of Authority Log)
- Training requirements for staffing

- Resources/Supplies needed
- IRB of Record and Costs
- Investigational New Drugs/Investigational Device Exemption (IND/IDE) Submissions with the U.S. Food and Drug Administration (FDA) (if applicable)
- Data Coordination Center needed for multiple sites (internal or external)
  - Database requirements many times are defined by funding agency
    - Internal Redcap or does it need to be Code of Federal Regulations (CFR) 21 Compliant?
      - Data Management and Monitoring plan (how often, what data points are being reviewed, remote vs in-person), implementation of statistical plan, Data Safety Monitoring Plan (DSMP), Medical Monitor, Data Safety Monitoring Board (DSMB)- this is important for budget
- Clinical Trial Coordination Center (internal or external)
  - Create study timeline, Payment of staffing, establishing contracts, progress reports, regulatory document management training of staff, Manual of Operations, purchase of supplies/equipment, communication to sites, recruitment oversight, Lab Manuals, Pharmacy Procedures, IRB Submissions
- Recruitment / Retention Program – MUST HAVE A PLAN
  - Study Branding- Decide short study name and how it will be referenced. Create a logo. Want something catchy for a busy coordinator to remember and easy to discuss with subjects.
  - Engage the Advocacy group in the design and materials for study dissemination (recruitment video, brochures, web postings)
- Multicenter Considerations
  - Publication guidelines
  - Ownership of data- delineation of staffing roles and responsibilities

TIP: This phase can last over a year, depending on the complexity of your research proposal. It is essential to utilize team science for submission success.

3. STUDY BUDGET

The Office of Sponsored Programs (OSP) provides guidance to assure proper stewardship of funds. Each College or Department may have a grants manager who will assist and advise you with the submission. The Office of Sponsored Programs is the group who provides the final sign off authorizing the submission on behalf of the University. That is why it is essential to communicate to both groups when you have a proposal.

There are two different agreements you can establish for people working outside of your university. Evaluate if you need to create **subawards** (agreements with another university for faculty or staff

working on a project; therefore the budget would need to include indirect costs from that institution) or a **consultant agreement** (person working privately does not include indirects, this might be used for a member on your data safety monitoring board who does not work regularly on the project, (i.e. meets twice a year for 3 hours each). Different paperwork and filing exist for each relationship and needs to be maintained throughout the study. Talk with your sponsored program officer to ensure you are using the correct pathway. https://go.osu.edu/consultant_agreement or https://go.osu.edu/subcontracts

Many NIH groups have an established disease specific network of sites created to help expedite the research endeavor (i.e. NeuroNEXT, Strokenet, SIREN, PECARN, PETAL, CTOT). Those networks have different restrictions on budget for submission so ensure you have done your homework.

Below are many of the costs to evaluate/consider when creating your budget.

Per Subject Costs consider the following:

- Consent (should include cost of time reviewing charts finding subject and scheduling the visit)
- Lab/Procedures
- PI effort, Specialty Physician, Research Nurse, Coordinator, Assistant Effort on each task of the schedule of events budget an hourly rate associated with staffing
- Data Entry/Query Resolution
- Subject meals, parking, stipend, travel
- Research pharmacy
- Hospital or room charges time and effort for lengthy study visits

☐ Site Costs including the following:

- Office and lab supplies/ shipping / dry ice

☐ One-time Costs can include the following:

- Start-up Fee (regulatory requirements- site study preparation and training)
- IRB Fee
- Long term documentation storage
- Ancillary Team prep costs (i.e. pharmacy, radiology, nursing unit)
- Study related supplies (i.e. Lab kits, license fees)
- Equipment (freezers, centrifuges, tubes)
- Recruitment and Advertising Costs, web site development (maintenance)

☐ Central Coordination Costs

- Screen failures
- Central pharmacy
- Outcomes equipment
- FDA Audit Fee per day (if applicable)
- Monitoring Fees to sites
- Medicare analysis fee (required at some sites)
- Document translation fee
- Protocol amendment costs
- Specialty training for project
- Serious Adverse Event (SAE) management
- Investigator Meeting/Update Meetings
- Fiscal Administration of the Study (subawards, consultant agreements, progress reports, paying sites)

- Overall study management

☐ Data Coordination Center Costs
  - Electronic Data Capture System Development and Management
  - Study Monitoring
  - DSMB members and their payment for service
  - Statistical Plan
  - Data review/analysis
  - Manuscript submission and preparation

☐ Indirect Costs- Site Indirect costs and those allowed on subawards (know rules when using existing network structures)

☐ Create Budget Justification for costs

☐ Multi-Site Trials - Establish the Study timeline and Payment Schedule- Metric established for sites to receive payment.

  - When paying multiple sites for clinical trials it is strongly recommended to pay fee for service. That way the site is paid for the work they complete and they are fiscally compensated for enrolling more patients.
  - Paying the sites the same amount of effort understand you **will** have sites that will overachieve and those that will under perform
    - Strongly recommend establishing good milestones for fund release; do not automatically pay without meeting recruitment targets/milestones.
  - Consider providing fiscal bonuses sites can receive for recruitment milestones (i.e. top enrolling site at close gets a monetary bonus and site with highest retention rate gets a monetary bonus). Track this during monthly calls to engage sites and provide a level of gamification for the trial

4. GRANT SUBMISSION

☐ It is imperative that you talk with the NIH contact or funding official prior to submission. The program officer assigned to the grant expects this contact. Have certain questions ready prior to calling to maximize obtaining the information you need for the submission.

https://grants.nih.gov/grants/planning_application.htm

☐ Double-check budget and have someone else review. Many times, the award comes in lower than your proposed budget.

  - Know what your bare bones budget is. You want people to still be involved in the study. If they are losing money performing the trial, it will hinder participation. Can you adjust the aims to still be adequately powered for what you want to investigate? *An underfunded study can be worse to facilitate than a study that was not funded at all.*

☐ Collect **NIH Biosketches** for all key personnel for NIH submissions

- Be sure you are using the current Biosketch form and reporting requirements.

☐ Get **Letters of Support**/ Create **Scopes of Work**

- Letters of support should be collected for important entities that intersect with your study. They should be on letterhead and convey their specific support for the study.
- If you are designating effort for staffing outside of your university. It is essential to create a scope of work separate from your protocol or manual for those individuals.
  - FTE (and calendar months)
  - What the individual will be doing (performance and deliverables) and within what timeframe
- Agreements with subcontractors and consultants should define a timeline and milestones for invoice payment. Establishing the milestones ensures those you are working with will be accountable for their roles/responsibilities on the study. (ie if there is a delay in study start-up certain groups do not receive payment for services that have not yet been rendered.)

☐ Submit for **IND/IDE**

It is important to understand the requirements for defining whether the study requires an IND (drug/biologic) or IDE (device/diagnostic). Always confer with a Regulatory specialist and the IRB (ORRP) before commencing your study planning, to be sure you do not have IND/IDE requirements. The FDA has produced guidance documents and decision charts to help determine this.

The CTSA has a Regulatory Manager who can assist with these tasks.

☐ Submit a request for funding (OSU PA-005) and initiation of a project. Notify BOTH your grants management office **and** the office of research, sponsored program office when you anticipate submitting a grant so they have it on their que for anticipated review and can meet the deadline. Both groups are essential in your project's submission success.

TIP: Many of the best grants take multiple submissions to be fully funded.

5. NOTICE OF AWARD

☐ After receiving word of potential funding. Write a **Project Management Plan** or a **List of Responsibilities (Appendix C)** ensure all parties know who is responsible for each task involved in the management of the trial. This is important for any intersection with pharmaceutical/device companies who may be providing study materials.

☐ Create **Study Start-up package** for sub-sites

☐ **Create Study materials**: worksheets, MOP, database, lab manual, specimen storage logs, data dictionary, Case Report Forms (CRF), drug accountability forms, IHIS smart phrases

☐ Start creating **Marketing Materials** that sites can use to help circulate information about the trial. Use of social media, get material created so it can be IRB approved at the initiation of the trial

- ☐ Adjust/Double check the budget/milestones of award with FTEs and the SOW you developed- adjust study timeline

- ☐ Put together a tracking checklist of the **Regulatory** documents needed by sites for activation- Maintain a Clinical Trial Master File of all sites documents and due dates of recertification. Can use an electronic regulatory system (Florence, Complion, Adverra). All studies must maintain the training documentation of staff working on the trial. Documents that can be included are:

    - Delegation of Authority Log or Study Staffing Listing (know who is IRB-approved to work on study for the life of the trial-)
    - FDA 1572 (Form for Drug studies that needs submitted to FDA)
    - Financial Disclosures
    - Protocol Signature Pages
    - Training documents of staff (Human Subjects, GCP, Protocol Training, IATA)
    - Monitoring documentation of the study
    - Investigative Brochure
    - Disposition of investigational product
    - IRB approvals
    - Communication
    - IND/IDE Submission

- ☐ Prepare **Training Materials** – These materials may include slide presentations, recorded webinars, newsletters, documents with specific learning objectives. Always record training session so later added staff can watch and verify training. Training is a GCP requirement to ensure all sites/staff/investigators are doing the study the same. Documentation of training is required with names and dates of attendance.

- ☐ Write and submit the Protocol and consent documents

- ☐ Create a **Manual of Procedures** (MOP) that tells exactly how to do certain tasks and it provides different forms used in the study for the study teams participating in the trial ensuring uniformity in tasks. Includes contact information and all details are in one area. Do not have five separate manuals for things and a bunch of different logins and locations. Centralize information/resources as much as possible. The MOP may include study-specific Standard Operating Procedures (SOP).

- ☐ Initiate paperwork needed for **Subawards** with sites. This can take longer than one might anticipate. And will require constant monitoring from sites on status.

    - CTSI has boilerplate language many sites have already agreed upon for https://ara4us.org

- ☐ Inform the Sponsored Program officer so the post award staff can start initiating the project fiscally

- ☐ Create **Clinicaltrials.gov** posting*

- ☐ Complete a management plan for the investigational new drug (IND) or investigational device exemption (IDE)-if applicable

- ☐ Create Site Initiation Plan, monitoring plan and documents (remote or in-person)

6. START-UP OF PROJECT

- ☐ Provide sites study start-up package with all created documents and supplies
- ☐ Confirm Receipt of all required regulatory documents from site prior to activate for enrollment
- ☐ Schedule Site Initiation Visit and Coordinator/PI training of protocol and database
- ☐ Provide Site with Activation Letter and official start date

7. MAINTENANCE AND CLOSURE

- ☐ Set-recurring status meetings to review important metrics: screening, enrollment, deviations, protocol issues, new training. It is important to keep sites and staff engaged.
- ☐ Track enrollment, protocol deviations/errors. Provide monthly reports to sites with this information and celebrate the success of sites who are working hard on the project.
- ☐ Sites that are doing well on the study have them present their tools of success. Perhaps it is a technique other sites could implement/emulate.
- ☐ Schedule Monitoring Visits and review reports for issues. Sites not performing well meet with them and evaluate how the coordination center can help.
- ☐ Payment of sites, subawards and consultants. Ensure people are following milestones and you do not get a giant invoice from someone at the end of the trial.
- ☐ Train New staff and obtain regulatory documents, manage and maintain current staff training documents.
- ☐ Ensure data is being reviewed and monitored **real time**- (nothing is worse than at the end of a three-year project and data managers- asking a question about the original consent)

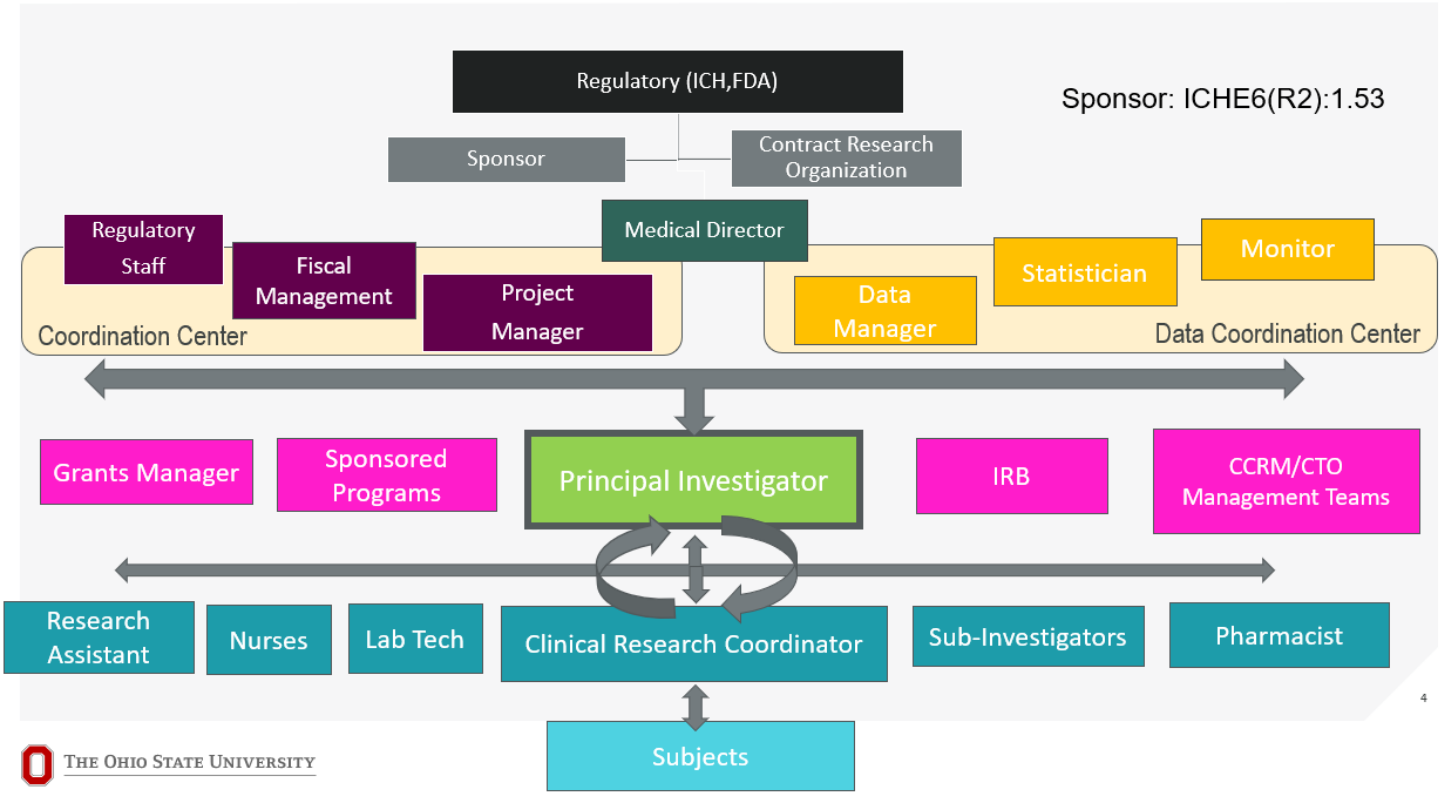
- ☐ Site Close out after all data is complete and all regulatory documents are current
- ☐ Get information about long term storage of documents from sites- who to reach out to? how to obtain (reference number)? and storage location?
- ☐ Inform sites about final payment.
- ☐ Provide study results to study team AND subjects before you publish the results. Keep IRB open to get results letter IRB approved include unblinding information

TIP: **The success of your study can be directly proportional to the level of PI supervision and frequency of effective staff meetings and metrics tracking.**

Glossary of Terms

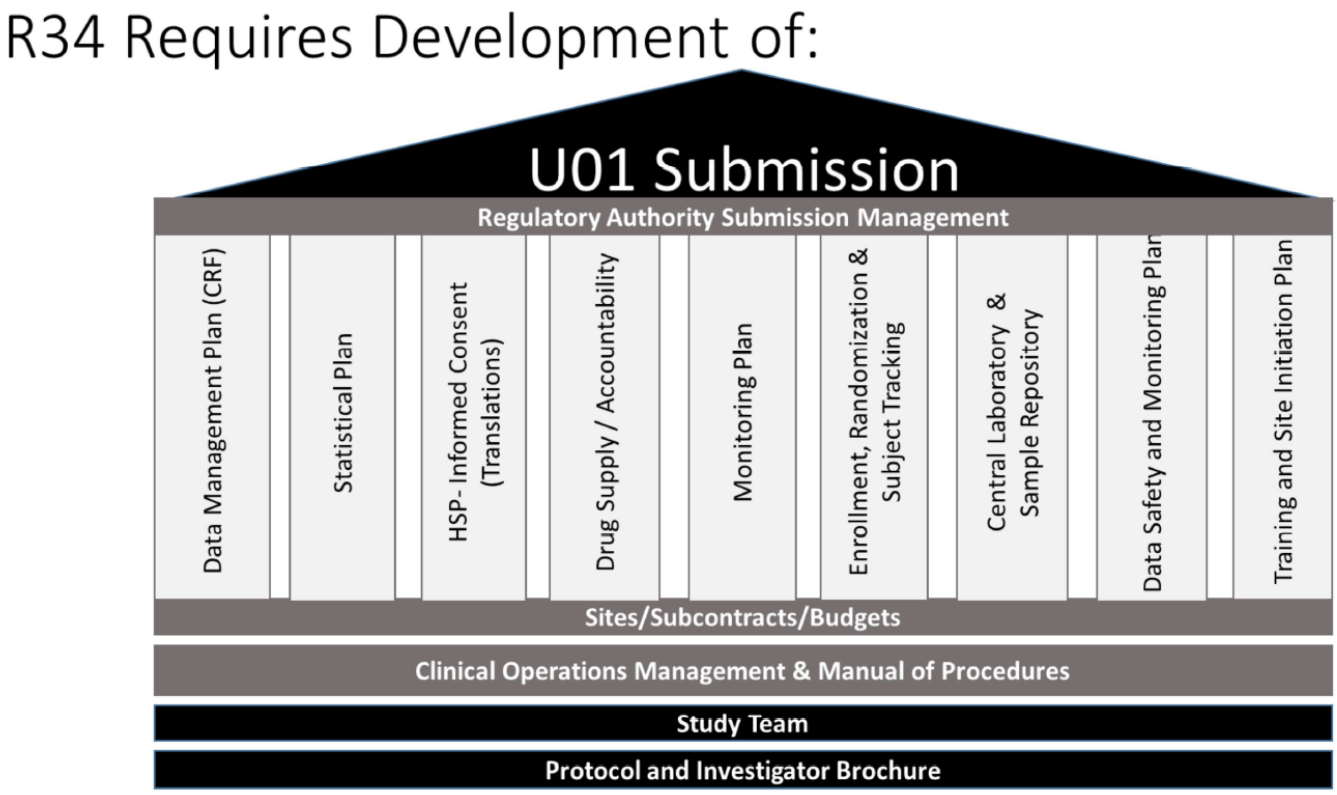
AE- Adverse Event
CCRM- Clinical Coordination and Research Management (formerly known as Clinical Trials Management Organization, CTMO) manages the Medical Center Pharmaceutical Trials
CCTRN- Cardiovascular Cell Therapy Research Network
CTSI- Clinical and Translational Science Institute at Ohio State and Nationwide Children's Hospital
CDA- Confidentiality Disclosure Agreement
CIRB-Central Institutional Review Board
CFR- Code of Federal Regulations
CRC- Clinical Research Center
CRF- Case Report Form
CTO- Clinical Trials Office- at OSU the Manage the Oncology Trials
CTOT- Clinical Trials in Organ Transplantation
DOA- Delegation of Authority
DSMB- Data Safety Monitoring Board
DUA- Data Use Agreement
ERIK- Enterprise for Research Innovation and Knowledge
FDA 1572 -Form for Drug studies that needs submitted to Food and Drug Administration
FTE- Full Time Effort
GCP- Good Clinical Practices
IATA- International Air Transport Association training for shipping dangerous goods
GMO- Grants Management Office
IDE-Investigational Device Exemption
IIT-Investigator Initiated Trial
IND- Investigational New Drug
IRB- Institutional Review Board
MOP- Manual of Procedures
MOO-Manual of Operations
MTA- Master Trial Agreement
NeuroNEXT- Network for Excellence in Neuroscience Clinical Trials
OSP- Office of Sponsored Programs
ORRP-Office of Responsible Research Practices
PECARN- Pediatric Emergency Care Applied Research Network
PETAL-Prevention and Early Treatment of Acute Lung Injury
PI- Principal Investigator
SAE-Serious Adverse Event
SIREN- The Strategies to Innovate Emergency Care Clinical Trials Network
SOP- Standard Operating Procedures
SPO- Sponsored Programs Office
RIT- Research Information and Technology

Appendix A: Clinical Research Team Structure



Appendix B: R34/U01 Clinical Trials Deliverables- Project Management

When planning a clinical trial through the NIH R34 mechanism, in addition to study design, investigators will prepare planning documents across multiple areas. These will be deliverables for the next funding milestone through a U01 Clinical Trial grant submission. Clinical research project managers can be key to organizing, writing, and editing these planning documents for you. For any clinical trial, the illustration below summarizes nicely the levels of project planning that is required. The use of a clinical research project manager is essential.



Appendix C: List of Responsibilities

Study:

Funder:

Key Responsibility	PI Team	Coordination Center	Data Center	Funding Group
1. Development of a Master Study Agreement and Budget agreeable to all parties				
2. Provide materials for the development of the protocol (NIH grant materials, product materials, earlier study reports, etc.)				
3. Development and approval of final protocol and informed consent form				
4. Development of data management plan				
5. Development of monitoring plan				
6. Development of case report forms				
7. Development of manual of procedures				
8. Development of pharmacy manual (if applicable)				
9. Identification of potential study sites				
10. Production and execution of protocol training webinars for sites				
11. Developing and executing subcontract agreements and statement of work and study budgets with study sites				
12. Collecting regulatory documents from study sites				
13. Shipping study supplies to study sites				
14. Performing training to sites on how to use study test article				
15. Providing shipping for study sites to send samples to the central lab (if applicable)				
16. Communication with sites and tracking study enrollments				
17. Tracking study metrics and report generation				
18. Issuing payments to sites for work performed				
19. Developing and managing a document filing and management system accessible to team (to be defined)				
20. Developing study electronic database				

21. Collection and tracking of study CRFs from sites (including a QA, internal monitoring and query resolution of CRF data)				
22. Developing a system for entry of case report forms to database				
23. Statistical analyses of study data				
24. Perform quality data review of cases, selecting and subcontracting with 4 investigators to be on this review committee				
25. Develop final report of study data				
26. Submit study reports to regulatory bodies (sponsors, FDA)				
27. Develop manuscript for publication of results				
28. Other?				
29. Other?				

By:_____ By:_____

Name: Name:

Date: _____ Date:_____

By:_____

Name:

Date: _____