Class Objectives

- Learn how to evaluate protocol feasibility
- Learn how to identify what you need to do as a study coordinator to get a study up and running here at OHSU and keep it running smoothly

“Protocol” Documents –

High

- Grants
- Investigator Contact
- Operations Manual
- Scientific Reviewers: NIH Foundation
- Co-Investigators
- Study Coordinators
- Laboratory Staff

Low

- Low Level Scientific Concepts
- May describe several studies
- Generally not revised
- May be reviewed with IRB approval

- IRB Member
- Statistician
- Auditors

- Low Level Scientific Concepts
- Generally describes one study
- May be reviewed with IRB approval

- IRB
- Statistician
- Auditors

Revisions require funding source approval

Protocols Contain:

- High Level Scientific Concepts
- Generally describe one study
- Moderate Level of detail
- May be revised with IRB approval

Operations Manual:

- Little or no scientific information
- High level of detail for completing tasks
- May be revised frequently without IRB approval (must be consistent with the IRB approved protocol)
Who Evaluates the Protocol?

- IRB: Subject Protection
- Funding agency (NIH, Foundation): $, Science
- Federal Oversight (FDA) if applicable: Protect Public Health
- Investigator: Feasibility, Scientific Interest
- Study Coordinator: Feasibility, Operational Implementation

Coordinator Protocol Review

- Learn the protocol requirements
- IRB application
- Write the consent
- Operational Implementation
  - Develop study checklists and data collection forms
  - Plan study workflow
- Feasibility

Protocol Analysis
Protocol Analysis

- Feasibility Analysis
- Operational Analysis
- Budget Analysis

- Who?
- What?
- Where?
- When?
- How?
- Why?

Feasibility Analysis

“No idea is so outlandish that it should not be considered with a searching but at the same time a steady eye.” – Winston Churchill

Feasibility Analysis

Why should we do a feasibility analysis?
- 2011 paper published about research at OHSU found that 31% of studies at OHSU enroll 0 or 1 subject
- Cost to institution $1 Million annually
- Underperforming studies slow down the entire research system
- Increases the risks of bad science

Early Feasibility Analysis

Initial Feasibility
- People (Who?)
- Time (When?)
- Protocol Requirements (What? and How?)

People
- Subjects
  - Do you have the subjects at OHSU?
  - Is the subject burden reasonable?
- Research Staff
  - Do you have enough staff to take on the study?
  - If not, can you afford to hire and train someone?
- Investigators
  - Do the investigators have the proper training?
  - Does the PI have access to the subjects?

Time
- Time to conduct the research
  - Need to make sure the PI has the time to supervise the study
  - Don’t want to take on the study if a PI is leaving OHSU before the end of the study
- Time to enroll subjects
  - Average 4 months from IRB submission to contract execution
  - Don’t take on studies if enrollment is expected to close within 8 months (if you have the subjects!)
Protocol Requirements

- Do you have the required equipment? Can you use it at OHSU?
- Does the OHSU Standard of Care match the protocol requirements and what the sponsor is willing to pay?
- Does the sponsor’s subject injury position conflict with OHSU’s?
- Do we do the required labs/tests here?

Identification of Standard of Care

- Standard of care varies from institution to institution so an OHSU PI or MD co-investigator makes determination (not the sponsor!)
- Not always obvious in the protocol
- Not always obvious to the MD
- Work with the CRBO if you have questions

Industry Sponsors/CROs

- Have you done studies with this sponsor/CRO in the past?
- How did it go? Were there contract problems?
  - ask around if you don’t have experience with the sponsor or CRO
How do I conduct a feasibility analysis?

- Feasibility Checklist available on the OCTRI website
  - [http://www.ohsu.edu/xd/research/centers-institutes/octri/resources/policies-forms/forms.cfm](http://www.ohsu.edu/xd/research/centers-institutes/octri/resources/policies-forms/forms.cfm)
  - You can modify the form to meet your needs.

Feasibility Scenarios

Operational Analysis

“Proper preparation prevents poor performance”
- Charlie Batch
Operational Analysis of a Protocol

• More detailed than the initial feasibility Analysis
• Ask what, who, where, when, how and why for every procedure listed in the protocol
• Also ask these questions for study management activities that aren’t listed in the protocol (DSMP activities, data entry)
• In the end you should have a road map for conducting the study

Example Asking the questions:
Identification of Labs

• Protocol states 20 mls of blood will be drawn at visit 2
  – Why are you drawing the sample?
  – What tubes do you need to draw?
  – What is the minimum amount of blood needed?
  – Does the sample need to be on ice?
  – Will the sample be processed at OHSU or at a central lab?
  – Does it need to be shipped that day?

Asking the questions: Identification of Unspecified Procedures

• Procedures required for safe conduct of a study aren’t always listed in the protocol
• Example: the protocol states a Dexa Scan will be completed at Visit 3
• What is a potential unspecified procedure for a Dexa Scan?
Asking the questions: Identification of Safety Procedures

- Safety Assessments
  - Which procedures are conducted for safety monitoring?
  - Are labs/procedures tied to safety endpoints?
  - Are there any special precautions for specific side effects, if required?

Asking the questions: Adverse Event Management

- Adverse Experiences
  - What are the expected adverse events?
  - Who will likely be the first study team member to learn of AEs? To whom do they report them?
  - What documentation is required and where will it be kept?
  - What Criteria are you using to grade severity?
  - What Criteria are you using to grade relatedness?
  - How long do I follow AEs?
    - After an adverse event - usually follow until event is resolved
    - UPs that occur within 30 days of last study intervention/subject discontinuation must be reported to the OHSU IRB

Asking the questions: Subject Discontinuation/Stopping Rules

- Subject Discontinuation criteria
  - How many subjects do you expect to drop out/or be withdrawn?
  - What study procedures need to be done?
  - Will you need to replace these subjects?

- Stopping rules/criteria
  - What is your review/communication process to make sure you follow your plan?
Where else should I look for information?

- OHSU IRB Initial Review Questionnaire (IRQ)
- Investigator Drug/Device Brochure
- Laboratory/Operations Manual
- Standard Operating Procedures (SOPs)
- Grant/Contract

What is in the Initial Review Questionnaire (IRQ)?

- IRQ information that may not be in the protocol:
  - Approved research staff
  - Funding information
  - # of subjects at OHSU
  - Recruiting and consenting procedures

What is in the IDB/Device Manual?

- The IDB (investigational drug brochure) contains information on the drug
- Study results to date
- All known adverse events and risks by body system
- Detailed information for the investigator on dosing
- Device Manual will include implant/compatibility/programming requirements
- Device Manual will include any calibration requirements
What is in a Lab/Operations Manual?

• Maybe known by other names
• Could include detailed information on almost anything
  – Lab processing
  – Case Report Form Completion
  – Patient flow during a visit (e.g. call ahead to see if X-ray is backed up before you head down there with a patient)
  – Calling and paying for a taxi
  – Many, many other details

What will I find in policies and SOPs?

• Institutional Policies describe how the hospital systems interact with the research systems at OHSU
• Departmental SOPs – describe who, what, where, when and how of research activities are conducted in a specific Unit/Department.
  – Obtaining/verifying informed consent
  – Drug accountability
• If you have SOPs you will be held to them in an audit so know them and follow them

What will I find in the Grant/Contract?

• Number of subjects in contract– what is the maximum # of subjects you can enroll?
• How and when do we get paid?
• How do we terminate the contract?
• Term of the contract/grant?
• Reporting Requirements to the sponsor
• Contracts must be signed by the appropriate OHSU institutional signatory (not the PI or Department) before the study can begin
Where Do I Start?

"Adventure is just bad planning" – Roald Amundsen

Implementing A Research Protocol

• Check Institutional Approvals
  – IRQ
  – Number of subjects you should request in the IRQ/ protocol is study dependent
    • Expected rate of attrition
    • Screen failure rate
    • Numbers need to be reasonable and consistent with the protocol and contract (when applicable)
  – Personnel
  – IRB-approved documents.
  – Regulatory binder updates
  – Working with a sponsor? Are your essential documents in? Are all current documents approved?
  – Non-English speaking patients/materials

Implementing A Research Protocol

• Review Protocol (Operational/Project management perspective)
  – Tool: Protocol Review Checklist or Study Start-up Task List
  – Intention of developing protocol SOP/checklists
    • Who, What, When, Where, Why, and How
    • Example: PI initiated study looking at attitudes towards new ultrasound machine through brief patient survey. Intent to enroll 140 pregnant women ages 18-35 at 9-28 weeks, receiving routine ultrasound at OHSU. Exclusion criteria: unable to provide informed consent.
Implementing A Research Protocol

• What Institutional resources do I need?
  – ECRIS
  – Research Rates (hospital services charged to the study account)
  – CRBO status change form
  – Industrial Account number
  – Interpreter services
  – Research store
  – Research pharmacy
  – Impacted departments/research groups
  – OCTRI, PCRO, WHRU, Knight Cancer Institute

Implementing A Research Protocol

• What are my equipment and supply needs?
  – Labs (shippers, tubes, spot cards, MD orders, lab slips, etc.)
  – Document storage (folders, binders, etc.)
  – Study equipment (Sponsor or Hospital)
  – CRFs (Sponsor or Department Template)
  – Questionnaires/Validated Instruments
    • Directions for administration and scoring
    • Contact for re-order

Implementing A Research Protocol

• What are my administrative needs?
  – Contact or process for patient reimbursement
  – Study alias for ordering supplies and shipping
  – Study tracking (enrollment, AIMS, labs)
  – Study ID and labelling
  – Templates (Fax, common communication)
  – Lab sheets/Downtime forms
  – Reporting process
  – Tracking study goal/AIMS
  – Managing training, competencies, and certifications
  – Managing equipment
Implementing A Research Protocol

• Do I have what I need for my recruitment plan?
  – IRB approved flyers/advertising
  – Templates for communicating with study subjects
  – Direction and maps
  – Medical records release forms
  – Referral process in place
  – Permission to Contact Form
  – Screening checklists
  – Consent process
  – Translated documents/short forms

Putting it into action!

1. Break-down visit 1 from protocol
2. Answer who, what, where, when, why, and how for procedures
3. Make a “To Do List”
Protocol Implementation

- Hurry-up, Wait, Go, Wait!

Training

- Verify study staff have training on Core Competencies
  - (see OHSU Clinical Research Coordinator Required training Checklist http://www.ohsu.edu/xd/research/centers-institutes/octri/resources/policies-forms/templates-checklists.cfm)
  - EPIC access/training, as required
  - ECRIS training, as required
  - EDC/RedCap/Data management

Training

- Staff protocol training
  - Make sure study staff read and understand the protocol
  - Have study staff acknowledge their roles in the study
  - Make sure study staff know how to identify and report deviations
  - Document that training was completed!
Work-flow planning

• Workflow planning is a balance between critical steps and Dependencies.
• What are the critical steps for a study activity?
  – Example: Enrollment 1) Review clinic schedule 2) Identify eligible patient 3) call and screen for eligibility 4) Invite for study visit if preliminarily eligible 5) Consent for participation
• What are these critical steps dependent on?
  – Example: 1) IRB approval/ WOA for recruitment plan 2) Appropriate training and access to EPIC for study staff 3) Database or log for screening 4) IRB approved Screening Script 5) Eligibility/Screening form 6) staff/process for scheduling 7) Availability of space

Work-flow Planning

• Workflow planning will need to accommodate changes in:
  – Protocol
  – Enrollment timeline
  – Institutional changes
  – Study staff
  – Data storage/reporting
• Reconciles protocol requirements with practical constraints of human subjects research.
• An essential component in documenting and evaluating study processes.

Common Workflow Problems

Don’t account for all the critical steps and/or dependencies related to study activities
  – Don’t forget regulatory/contractual timelines!
Leads to:
• Enrollment issues
• Regulatory / Non-Compliance Issues (Protocol Deviations, adverse events)
• Patient safety concerns
• Poor data integrity
Avoiding Poor Workflow Planning

- Understand the protocol and institution you are working within
  - Examples: Scheduling, office space, shipping deadlines, CRBO updates, etc.
- Understand your patient population:
  - Illness, mobility, socio-economic concerns, mental health, availability, familiarity with institution or research process, motivation for participation, language, etc.
- Establish workflow processes that work for your team
  - Ask for what you need – PI, Sponsor, Institution, Study subjects!
  - Be adaptive
- Have a documented workflow process and communicate changes in systematic way.

OHSU Tools and Forms

- OCTRI has compiled a list of research related forms and templates that may be useful for you:
  - [http://www.ohsu.edu/xd/research/centers-institutes/octri/resources/policies-forms/forms.cfm](http://www.ohsu.edu/xd/research/centers-institutes/octri/resources/policies-forms/forms.cfm)
    - Including: EPIC access, Research Rates, CRBO forms
  - Research Admission - request form available at [http://www.ohsu.edu/research/crp/docs/researchFYI.doc](http://www.ohsu.edu/research/crp/docs/researchFYI.doc)
  - Research Outpatient Appointment Scheduling Request [http://www.ohsu.edu/xd/research/centers-institutes/octri/resources/policies-forms/ohsu-research-policies.cfm?WT_rank=1](http://www.ohsu.edu/xd/research/centers-institutes/octri/resources/policies-forms/ohsu-research-policies.cfm)
    - It is necessary to have the research association set prior to scheduling the patient’s first research appointment

OHSU Tools and Resources.

- Use of Research Devices and Equipment
  - [http://ozone.ohsu.edu/clinicalengineering/eqpPolicies.cfm](http://ozone.ohsu.edu/clinicalengineering/eqpPolicies.cfm)
    - Must be inspected by Clinical Technology Services if the device/equipment was not purchased by OHSU
- Computers
  - If the sponsor provides you with a computer for the study (not purchased through OHSU) it must be inspected by ITG
OHSU Tools and Forms

• Follow OHSU Research and Hospital Policies:
  – IRB Policies: http://www.ohsu.edu/xd/about/services/integrity/policies/

Conducting the Protocol

• Once the study has IRB approval the study team is expected to adhere to the protocol without deviations – unless it is for the safety of the subject

Prediction is very difficult, especially if it's about the future.

Niels Bohr
Protocol Analysis

Evaluate! Re-evaluate

• Once your studies are up and going, put in place a plan to evaluate the recruitment and study conduct (every 3-6 months)
• If enrollment isn’t going well ask yourself why? Is there anything you can do?
• If you are having a lot of protocol deviations and you won’t meet your endpoints look at your operational analysis to see if there is something you can change
• If you don’t think you can turn the study around as designed the PI should consider stopping it.

Revising the Protocol

• Protocol Modifications
  – An amendment/modification can be submitted for IRB approval to address new information/difficulties
  – Strive to minimize modifications so that data remains “poolable” by completing a good analysis
    • Don’t want to compare apples and oranges
  – Maintain consistency within and between the protocol, consent, and procedure manuals (avoids confusion)
Protocol Revisions, cont.

- Modifications
  - You may want to re-analyze your protocol if there are significant changes before you submit the modification to the IRB but you should always analyze new procedures before implementation
  - Feasibility
  - Location/Scheduling
  - Training
  - Budget

Stopping a Study

- If you determine you won’t be able to address the recruitment or other problems and want to stop the study:
  - Industry sponsored
    - PI must notify the sponsor in writing
    - Let the Clinical Trials Office and SPA know
  - NIH sponsored research
    - PI should contact program officer to look at options (Your PI should have a plan, e.g. adding sites, protocol modifications)
    - Notify RGC
  - Submit modification to change study status in the eIRB

What about budget feasibility?

- Budget Development Training available
- Research Administration Training and Education (RATE)
- [http://www.ohsu.edu/xd/research/administration/training-and-education-rate/classes-workshops/index.cfm](http://www.ohsu.edu/xd/research/administration/training-and-education-rate/classes-workshops/index.cfm)