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The Role of the Principal Investigator

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What it means to be a Principal Investigator

- The Principal Investigator (PI) is the individual responsible and accountable for conducting the study.
- The PI must protect the rights and welfare of human subjects
- The PI assumes full responsibility for the treatment and evaluation of human subjects, and for the integrity of the research data and results.
- The PI needs complete understanding of regulations and guidelines for conduct and implementation of the study protocol, including Federal, State, and local regulations and policies, as well as certification requirements including IRB, Conflict of Interest Disclosure, Human Subject Protection and Good Clinical Practice certifications.
- https://www.fda.gov/media/77765/download
- https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf
- https://www.youtube.com/watch?v=hTBPIg2qPuA

What is the PI responsible for?

Charged to conduct objective research that generates independent, high quality, and reproducible results.

Management and integrity of the design, conduct, and reporting of the research project and for managing, monitoring, and ensuring the integrity of any collaborative relationships.

The direction and oversight of compliance, financial, personnel, and other related aspects of the research project and for coordination with school, department, and central administration personnel to assure research in is conducted in accordance with Federal regulations and University and sponsoring agency policies and procedures.

Scope of PI responsibilities

- Scientific
  - Conduct of Research
  - Preparation of scientific proposals
  - Protocol Preparation and review
- General Administrative
  - Space and Equipment management
  - Reporting
  - Project Closeout
  - Proposal budgets

Investigator oversight

- It is a requirement under ICH GCP E6 (R2) addendum for the Principal Investigator (PI) to demonstrate their oversight of a clinical trial. Sites need to be able to provide evidence that the PI is actively involved in the conduct of the trial and is assuming the required responsibilities. As they are considered personally responsible for conducting and supervising the conduct of all trial activities the PI should have a plan for the supervision of all staff working on the trial. The delegation log is not a paper exercise, the PI needs to be able to support their actions if questioned.
- Be present, engaged, and knowledgeable

Examples of PI oversight

- Lead study team meetings
- PI plan for team supervision
- Engaged in recruitment
- Review and sign off AEs and SAEs
- Review lab results to identify trends in abnormal values
- Knowledgeable of the protocol
- Engaged in study visits
- Know who is on the delegation log and why
- Know where the data is located
- Know (and ensure) the study records are in order

ICH-GCP (human subject research)

- Protecting the safety, rights, and well-being of human subjects
- Conducting the study in accordance with current protocol
- Personally conducting or supervising the investigation
- Reporting the adverse events in accordance with federal regulations
- Following federal regulations and requirements for obtaining informed consent
- Ensuring that the Federal IRB requirements are met
- Maintaining adequate and accurate records and making them available for audit
- Promptly reporting to the IRB any changes or risks to human subjects
- Complying with all other requirements and investigator obligations specified in the federal regulations

Follow the protocol

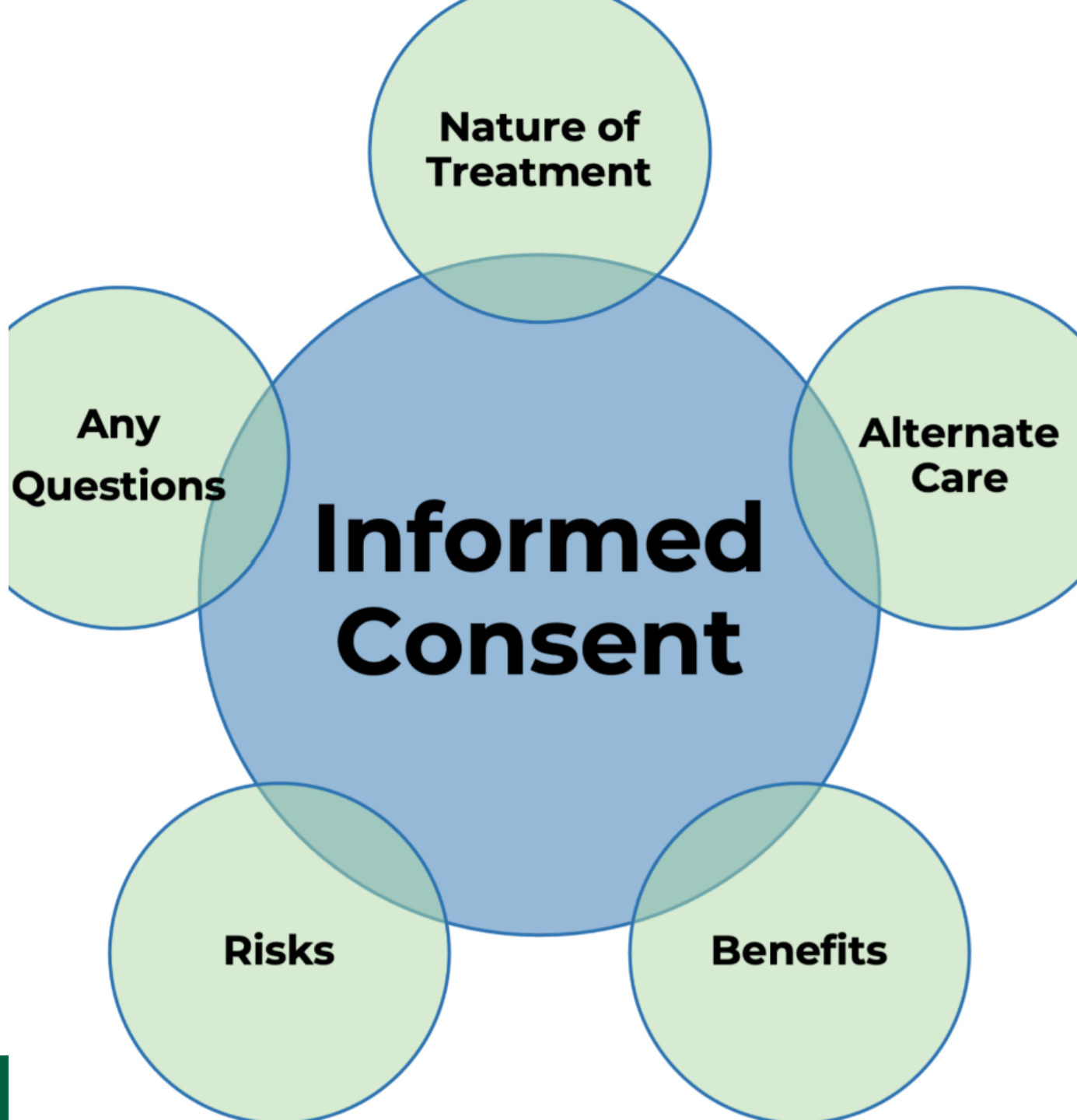
- Eligibility
- Study visits and assessments
- Study timelines
- Study dosing
- Study concomitant medication restrictions
- Study endpoint collection

Personally conduct/supervise the study

- Know the protocol
- Available and involved
- See the patients
- Review documents
- Know what the staff is doing
- Recruit, consent
- Know the protocol metrics

Informed Consenting and IRB

- Inform participants that activities are for investigational purposes
- Ensure informed consent – 21 CFR Part 50
- IRB requirements – 21 CFR Part 56



Adverse Event Reporting

- Report adverse experiences to sponsor
- Follow 21 CFR 312.64 regarding AE reporting requirements, definitions, timelines
- Have read and understand investigator brochure
- Knows all potential risks and side effects
- PI attributes level of AE and causality
- Expected or unexpected and/or serious

Train and inform study team

- Ensure all study associates, colleagues, employees assisting in the study:
  - Informed about regulatory obligations
  - Provide adequate training/education to accomplish assurance
  - Document how this is “ensured”

Maintain adequate/accurate records

- Follow 21 CFR 312.62 regarding data management and recordkeeping
- Understand source documentation
- Make records available for inspection in accordance with 21 CFR 312.68
  - Paper records
  - Electronic records
  - Case report forms

IRB Approvals and Communication

- Ensure that the IRB is in compliance with 21 CFR Part 56
- Obtain initial and continuing reviews & approvals
- Promptly report to IRB all changes in research activity AND all unanticipated problems involving risks
- Obtain IRB approval for any changes in protocol

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A successful investigator

How to be an active investigator

- Engage in educational and training programs, professional organizational conferences.
- Network with experienced investigators
- Find a mentor
- Serve as a sub-investigator on a study/trial
- Look for available trials
- Establish realistic expectations
- Create a realistic recruitment plan

How to be an active investigator (cont.)

- Plan adequately before committing to a trial
  - Assess feasibility
  - Assure a sufficient population
  - Fully understand a PI's roles and responsibilities
  - Assemble qualified, experienced study staff

Challenges for Investigators

- Trial finances
- Time required to implement the trial
- Data safety reporting
- Workload balance
- Biostatistics
- Oversight
- Mentorship

Factors in investigator success

- Experienced, well-trained staff
- Personal commitment
- Strong work ethic
- Institutional support
- Ability to recruit participants
- Business knowledge and experience
- Ability to network effectively
- Collaborative

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Resources

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Data safety and management

Responsible Conduct of Research (RCR)

- RCR is critical in maintaining the ethical conduct and preserving research integrity of academic endeavors
- Training is required by UAB
  - https://www.uab.edu/research/home/uab-rcr-training/faculty-staff

Research Data Management

- Investigators are required to submit data management plans (DMPs) with federal grant proposals.
  - Strongly encourage DMPs for all projects
- Consider:
  - I'm starting to work on a grant application to a federal agency. What kind of data management plan do I need to include?
  - Where can I find examples of data management plans?
  - What are some of my options for depositing my data?
  - What UAB resources are available to help me with managing my data?
- https://www.uab.edu/faculty/rdm
- https://www.youtube.com/watch?v=N2zK3sAtr-4

Data Safety & Security

- Be familiar with the UAB Data Protection Rule
  - https://www.uab.edu/it/home/policies/data-classification/data-protection-rule
  - Store data on a UAB secure server
  - DO NOT put data on your laptop, jump drive or external hard drive
  - RedCap is an excellent database software system
  - Ensure the system you are using meets all the UAB requirements.
    - https://www.uab.edu/it/home/policies/data-classification/classification-overview

	Public	Sensitive	Restricted/PHI
UABFile Share	✔	✔	✔
Desktop C Drive	✔	– password required; encryption optional.	✖
Laptop C Drive	✔	– password required; encryption optional.	– password/pin and encryption required.
UAB Box	✔	✔	– Risk assessment required.
Personal accounts	✔	✖	✖
Thumb Drive	✔	– encryption required.	✖
Mobile Device	✔	– device password/pin and encryption required.	– device password/pin and encryption required.
UAB Email	✔	– only to uab.edu or uabmc.edu email addresses.	✖
UABMC Email	✔	– only to uab.edu or uabmc.edu email addresses.	– requires third-party encryption tool to send externally.

Data Management

- Be in compliance
- Ensure data is
  - Accessible
  - Shareable
  - Reproducible
- Be consistent in data collection (naming conventions)
- Perform regular data audits
- Use the right tools (a data management system)
- Engage a biostatistician early in the process

Resources

- Office of Sponsored Programs
  - https://www.uab.edu/research/home/osp-researchers-toolkit
- Institutional Review Board
  - https://www.uab.edu/research/home/investigators
- Investigator responsibilities
  - https://www.youtube.com/watch?v=czi48Btd5Cc
  - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3097692/
  - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7122254/

CCTS

- **Center for Clinical and Translational Sciences**
  - https://www.uab.edu/ccts/
  - SO MANY resources available from CCTS
    - **Research Commons** (Grant Help, Grant Library, Informatics, BERD, Project Panel Review, etc) https://www.uab.edu/ccts/research-commons
    - **Training Academy** (Grant resources, mentoring) https://www.uab.edu/ccts/training-academy
    - **Clinical Translational** (trainings, feasibility, budget, SOPs, etc) https://www.uab.edu/ccts/clinical-research
  - They host frequent trainings on various topics throughout the month