

Roles & Responsibilities of the Research Team



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Agenda

- Investigator
 - OHRP
 - FDA
 - ICH CGP guidelines
 - NIH
- Sub-investigators
- Participant
- Research Nurse Specialist
- Clinical Research Nurse in CC
- Clinical Data Manager
- Pharmacists
- Professional Organizations

OHRP's Use of "Investigator" ...

- Any individual who is involved in conducting human subjects research studies including:
 - obtaining information about living individuals by intervening or interacting with them for research purposes;
 - obtaining identifiable private information about living individuals for research purposes;
 - obtaining the voluntary informed consent of individuals to be subjects in research; and
 - studying, interpreting, or analyzing identifiable private information or data for research purposes.

...OHRP's Use of "Investigator"

- Investigators can include physicians, scientists, nurses, administrative staff, teachers, students
- Multiple investigators, 1 investigator is designated the "principal investigator" with overall responsibilities for the study
- Learn more: [OHRP's Investigator Responsibility Frequently Asked Questions](#)



Investigator Responsibilities...

- Design and implement ethical research, consistent with three ethical principles delineated in the Belmont report
- Comply with all applicable federal regulations impacting the protection of human subjects
- Ensure that all research involving human subjects is submitted to and approved by the appropriate institutional review board



...Investigator Responsibilities...

- Comply with all applicable IRB policies, procedures, decisions, conditions, and requirements
- Implement research as approved and obtain prior IRB approval for changes
- Obtain informed consent and assent in accord with federal regulations and as approved by the IRB
- Document informed consent and assent in accord with federal regulations and as approved by the IRB



...Investigator Responsibilities

- Report progress of approved research to the IRB, as often and in the manner prescribed by the IRB
- Report to the IRB any injuries, adverse events, or other unanticipated problems involving risks to subjects or others
- Retain signed consent documents and IRB research records for at least 3 years past completion of the research activity

FDA and the Role of the Investigator

- Overall responsibility for the conduct of the clinical trial
 - Clinical Investigator
 - PI in the protocol document
- Other Investigators are referred to as Subinvestigators
- Refer to 21 CFR Parts 11, 50, 54, 56, 312, and 812 for a more comprehensive listing of FDA's requirements

Role of the Investigator: Drugs or Biologics

- An investigator's responsibilities in conducting clinical investigations of ***drugs*** or ***biologics*** are provided in [21 CFR Part 312](#)
 - Many of these responsibilities are included in the required investigator's signed statement, [Form FDA-1572](#)
 - Page 2, Section 9 lists the commitments of the Investigator



Investigator Commitments...

- Conduct study in accordance with the relevant, current protocol and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, right, or welfare of subjects
- Personally conduct or supervise the described investigation



...Investigator Commitments...

- Inform any patients, or any persons used as controls, that the drugs are being used for investigational purposes and ensure requirement relating to obtaining informed consent in [21 CFR Part 50](#) and IRB review and approval in [21 CFR Part 56](#) are met
- Agree to report to sponsor adverse experiences that occur in the course of the investigation in accordance with [21 CFR 312.64](#)



...Investigator Commitments...

- Read and understand the information in the investigator's brochure, including the potential risks and side effects of the drug
- Agree to ensure all associates, colleagues, and employees assisting in the conduct of the study are informed about their obligations in meeting the previous commitments



...Investigator Commitments...

- Maintain adequate and accurate records in accordance with [21 CFR 312.62](#) and to make those records available for inspection in accordance with 21 [21 CFR 312.68](#)
- Ensure that an IRB that complies with the requirements of 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the clinical investigation
 - Promptly report to the IRB all changes in research activity and all unanticipated problems involving risks to human subjects or others.
 - Make no changes in the research w/o IRB approval except where necessary to eliminate apparent immediate hazard to human subjects.



...Investigator Commitments

- Comply with all other requirements regarding the obligation of clinical investigators and all other pertinent requirements in 21 CFR Part 312

Form 1572

- Form 1572 is updated as needed
- All copies of the Form 1572 are to be maintained in the regulatory binder
- FDA's 2010 [Information Sheet](#): *Guidance for Sponsors, Clinical Investigators, and IRBs: Frequently Asked Questions—Statement of Investigator (Form FDA 1572)*

FDA Guidance

- [FDA 2009 guidance document](#) provides an overview of the responsibilities of a person who conducts a clinical investigation of a drug, biological product, or medical device (an investigator as defined in 21 CFR 312.3(b) and 21 CFR 812.3(i)).
- Provides information for the Investigator on:
 - Supervisory activities associated with the conduct of a clinical trial including:
 - What is appropriate delegation of study-related tasks
 - What is adequate training
 - What is adequate supervision of the conduct of ongoing clinical trial
 - What are Investigator's responsibilities for oversight of other parties involved in the conduct of a clinical trial?
 - Protecting the rights, safety , and welfare of study subjects
 - Reasonable medical care
 - Reasonable access to medical care
 - Protocol violations that present unreasonable risk
- ALL research team members should review this document.

Role of the Investigator: Devices

- An investigator's responsibilities in conducting clinical investigations of a **medical device** are provided in [21 CFR Part 812](#), including the requirement that there be a signed agreement between the investigator and sponsor (see 21 CFR 812.43(c)(4) and 812.100).
- Device regulations do not require the use of a specific form for an investigator's statement

GCP and the Investigator

- Investigator qualifications & agreements
- Adequate resources
- Medical care of trial subjects
- Communication with the IRB
- Compliance with protocol
- Investigational product
- Randomization procedures and unblinding
- Informed consent
- Record and reports
- Safety reporting
- Premature termination of trial
- Final report

ICH GCP E6: Investigator Qualifications & Agreements

- The Investigator should:
 - Be qualified (documented) by education, training & experience to assume responsibility for proper trial conduct
 - Be familiar with the appropriate use of the investigational product, IB, and other information provided by sponsor
 - Be aware of, & should comply with, GCP and the applicable regulatory requirements
 - Permit monitoring, auditing and inspection
 - Delegate duties to appropriately qualified persons

ICH GCP E6: Adequate Resources

- The Investigator should:
 - Demonstrate adequate potential for recruitment
 - Have sufficient time for trial conduct and completion
 - Have adequate staff and facilities to conduct the trial
 - Ensure training to staff

ICH GCP E6: Medical Care of Trial Subjects

- The Investigator should:
 - Ensure that qualified physician investigators/sub investigators for the trial, should be responsible for all trial related medical decisions
 - Adequate medical care during and after trail participation
 - Make reasonable efforts ascertaining for premature withdrawal from trial
 - Inform subject's primary physician about the subject's participation in the trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.

ICH GCP E6: Communication with IRB

- The Investigator should:
 - Seek written & dated approval for trial protocol, informed consent document, recruitment procedures, etc. prior to trial initiation
 - Provide latest copies of Investigator Brochure (IB) to IRB
 - Provide all relevant documents for review during trial

ICH GCP E6: Compliance with Protocol

- The Investigator should:
 - Conduct trial in accordance with the protocol version agreed & documented by the sponsor, IRB and regulatory authority
 - Ensure that no changes are allowed in the protocol except in case of immediate hazard to the patient

ICH GCP E6: Investigational Product

- The Investigator:
 - Is responsible for investigational product accountability at the site
 - May be assigned to pharmacist/individual
 - Ensure that investigational product is stored as specified by sponsor or regulatory authority
 - Ensure that the investigational product is used only in accordance with the protocol

ICH GCP E6: Randomization Procedures and Unblinding

- The Investigator:
 - Should follow the trial's randomization procedure
 - Report any premature unblinding to be explained to sponsor

ICH GCP E6: Informed Consent..

- The Investigator should:
 - Comply with regulatory requirement, GCP and ethical principles
 - Document communication of revised consent document to IRB and patient
 - Not influence or coerce subject to participate
 - Ensure that the subject or their legal representative is fully informed in their own language
 - Review Subject's responsibilities as part of the informed consent process

... ICH GCP E6: Informed Consent

- The Investigator should:
 - Ensure that the informed consent document does not contain technical language
 - Allow ample time for the consent process and opportunity for exchange of information or subject questions
 - Provide an impartial witness for illiterate patients
 - Provide the Subject with a copy of the signed and dated Informed Consent Document

ICH GCP E6: Records and Reports

- The Investigator:
 - Should ensure accuracy, completeness, legibility and timeliness of data to sponsor in CRF
 - Ensure corrections on a CRF be signed and dated
 - Should maintain trial related documents
 - Ensure all financial agreements are in place prior to subject enrollment
 - Provide access to records by monitor, regulatory agency or auditors
 - Submit progress reports to IRB

ICH GCP E6: Safety Reporting

- The Investigator should:
 - Report all serious adverse events, including deaths, to sponsor and IRB/regulatory agency as per SOPs

ICH GCP E6: Premature Termination of Trial

- The Investigator should:
 - Inform subjects
 - Assure therapy and follow up
 - Inform sponsor, IRB, and other regulatory authorities as per SOPs

ICH GCP E6: Final Report

- Upon completion of the study, the Investigator should provide the IRB and other regulatory authorities with a summary of the trial's outcome

NIH: Principal Investigator (PI) (SOP #19)

- Must be NIH employee
 - qualified members of the credentialed CC senior, junior, research or adjunct staff, registered nurses, pharmacologists, psychologists, or other health professionals
 - Consultants, contractors, and students **may not** act as principal investigators
- Only 1 PI per protocol
- Responsible for:
 - designing, conducting, and monitoring protocols
 - ensuring the protection of human subjects
 - overseeing the informed consent process
 - overseeing the integrity and analysis of research data
 - prevention of conflicts of interest by all AIs
 - assuring that protocols are followed and that data are collected promptly and accurately.
 - ensuring necessary approvals are obtained

Sub-Investigator

- "Any individual member of the clinical trial team designated and supervised by the investigator at a trial site **TO PERFORM CRITICAL TRIAL-RELATED PROCEDURES AND/OR TO MAKE IMPORTANT TRIAL-RELATED DECISIONS** (e.g., associates, residents, research fellows)."
 - *Per FDA's official guidance, the "ICH E-6 Good Clinical Practice: Consolidated Guidance"*
- Include in block #6 of the Form FDA 1572

NIH: Associate Investigators (AI)

- 2 types of Associate Investigators:
 - **Lead Associate Investigator (LAI)**
 - Individual who plays a leading role in the formulation, writing, and implementation of a clinical research protocol under the mentorship of the protocol's principal investigator
 - May be a physician, a dentist, a Ph.D., an RN, a member of the allied health professions, or a trainee
 - 1 per protocol
 - **Associate Investigator(s) (AI)**
 - Individual(s), other than the PI and LAI who makes substantial contributions to the conception and design of the study, or to the acquisition of data, or to the analysis and interpretation of data
 - Contractors may serve as AIs
 - May be several AIs on a protocol

Study Subject's Responsibilities...

- Respect research staff and other participants
- Read the consent form and other documents
- Ask questions if they do not understand something about the study, their rights and responsibilities
- Carefully weigh the risks and benefits when deciding whether to participate in the study
- Refrain from signing the consent document until they understand its content and feel comfortable with their decision to participate

Taken from: Resnik, D.B. & Ness, E. (2012). Participants' responsibilities in clinical research. *Journal of Medical Ethics* 38(12), 746-750.

...Study Subject's Responsibilities...

- Follow directions for all protocol related procedure include those associated with self-administered study medications
- Know when the study begins and ends.
 - Particularly important for an intervention trial that has a follow-up period after the intervention is completed
- Show up at scheduled appointments on time, and inform the staff within a reasonable time if they need to reschedule

Taken from: Resnik, D.B. & Ness, E. (2012). Participants' responsibilities in clinical research. *Journal of Medical Ethics* 38(12), 746-750.

...Study Subject's Responsibilities...

- Provide truthful answers to questions asked throughout the study
- Inform staff if other medical care is needed while on the study
- Inform the staff if there are questions they would rather not answer
- Report pain, discomfort, nausea, dizziness and other problems and symptoms they experience during the study.

Taken from: Resnik, D.B. & Ness, E. (2012). Participants' responsibilities in clinical research. *Journal of Medical Ethics* 38(12), 746-750.

...Study Subject's Responsibilities

- Keep information about the study confidential, if asked to do so
- Keep staff informed when contact information changes
- If they decide to withdraw from the study, inform the staff and follow the procedures for withdrawal

Taken from: Resnik, D.B. & Ness, E. (2012). Participants' responsibilities in clinical research. *Journal of Medical Ethics* 38(12), 746-750.

Nurses

- At NIH, there are 2 main clinical research roles for nurses
 - Clinical Research Nurse (AKA: Staff Nurse)
 - Spends the majority of their time delivering direct care to research participants and their families
 - Research Nurse Specialist (AKA: Clinical Trial Nurse, Clinical Research Nurse, Research Nurse Coordinator)
 - Spends the majority of their time in the managing the study, coordinating within the multidisciplinary team, communicating with referring physicians and providing for protection of human subjects

Research Nurse Responsibilities...

- Licensure responsibilities
- Coordinate study:
 - Recruiting
 - Screening and scheduling patients
 - Securing informed consent
 - Study conduct
 - Initiation, monitoring and close-out visits
 - Coordination of lab pick-ups, supplies
- Maintain integrity of protocol
- Maintain regulatory files

...Research Nurse Responsibilities...

- Assist PI in preparing protocols & consent for initial review, continuing review & amendments
 - Timely submissions
 - Meets the regulatory requirements
 - Accurate data
- Report adverse events expeditiously
 - Timely, complete
- Maintain participant records & documentation
- Clinical care, drug prep & administration
- Data management & QA

...Research Nurse Responsibilities...

- Teach patients
- Teach staff
- Abstract, analyze & publish findings with PI
- Stay informed (with PI) of new information regarding investigational agent
 - Investigators Brochure, Articles, IND Safety Reports, Memos
- Prepare & facilitate monitoring of trials
 - Resolve discrepancies, common goals/time lines

...Research Nurse Responsibilities

- Anticipate the deadlines & data needed
 - IRB
 - FDA
 - Professional meeting abstracts
 - Audit/monitoring visits
- Review previous publications & reports
 - Data tables, charts, graphs, scan images
- Mentor other research nurses

Clinical Trials Nurse (CTN)

- ONS CTN competencies, the research nurse specialist “demonstrates critical thinking and implementation of the nursing process, thus providing leadership in the conduct of clinical trials, improving outcomes for patients, and enhancing study integrity.”
- Accomplished through competent practice in the following functional areas:
 - Protocol compliance
 - Clinical Trials–Related Communication
 - Informed Consent Process
 - Management of Clinical Trial Patients
 - Documentation
 - Patient Recruitment
 - Ethical Issues
 - Professional Development

Study Coordinator

- Similar to the Research Nurse minus the licensure responsibilities
- Will vary, sometimes more regulatory versus clinical

Staff Nurse

- Provides direct patient care including treatment and patient education
- Adheres to protocol
- Collects specimen as per protocol
- Documents all patient encounters in the medical record
- Informs PI/Research Nurse Specialist of patient or protocol related issues/concerns
- NIH: Job title is a Clinical Research Nurse (CRN)
 - competencies have been developed based on [Domains of Practice](#)
 - *Fundamentals of Clinical Research for the Clinical Research Nurse*

Clinical Data Manager (CDM)

- Individual responsible for some or all activities related to Clinical Data

Management:

- Data acquisition/collection
- Data abstraction/extraction
- Data processing/coding
- Data analysis
- Data transmission
- Data storage
- Data privacy/confidentiality
- Data QA

Pharmacist

- PI is ultimately accountable for drug accountability
- Often delegated to a pharmacist:
 - Prepares drugs as per protocol
 - Stores investigational products as per protocol
 - For multiple studies using same IND agent, needs to provide separate/distinct storage in pharmacy
 - Maintains accurate drug accountability records
 - Receipts of drug shipment/invoices
 - Drug accountability record forms/database

NIH Learning Opportunities

- CT seminar series
- Protocol Navigator seminar series
- Team and IC meetings
- Grand Rounds
- Yellow sheet
 - <http://calendar.nih.gov/app/MCalWelcome.aspx>

Professional Organizations

- Disease specific
- Association of Clinical Research Professionals (ACRP)
- International Association of Clinical Research Nurses (IACRN)
- Oncology Nursing Society Clinical Trials Nurse Special Interest Group (ONS CTN SIG)
- Society for Clinical Research Associates (SoCRA)
- Public Responsibility in Medicine and Research (PRIM&R)
- Society of Clinical Data Managers (SCDM)

Association of Clinical Research Professionals (ACRP)

- International association (>18,000; members >70 countries)
- Established in 1976
- Provide education and networking
- Target clinical research professionals in industry and in hospital, academic medical centers and physician office settings.
- <http://www.acrpnet.org/>

International Association of Clinical Research Nurses (IACRN)

- International professional nursing organization (<257 members; >5 countries)
- Established in 2007
- Dedicated to supporting educational and professional needs of clinical research nurses
- Developing professional standards and best practices to ensure quality research practices, high ethical standards, regulatory compliance, and human subjects' protection.

<http://iacrn.memberlodge.org/>

Oncology Nursing Society Clinical Trials Nurse Special Interest Group (ONS CTN SIG)

- Community within the Oncology Nursing Society for members to share ideas, information, and experiences
- Established in 1990
- >900 members
- Offers educational sessions at conferences
- Maintains a virtual community with online resources
- Published a *Manual for Clinical Trials Nursing*
- Developed:
 - [Oncology Clinical Trials Nurse Competencies](#)
 - Interactive [webcourse](#) for oncology nurses new to clinical trials
- <http://ons.org/Membership/SIGs/Listing/SIGDetails?SigCode=CTN>

Public Responsibility in Medicine and Research (PRIM&R)

- Established in 1974
- Serves array of individuals and organizations involved in biomedical, social science, behavioral, and educational research
- >3,600 members individuals
 - Professionals working with human subject protections, animal care and use, institutional biosafety programs, RECs, and ESCROs including
 - HRPP/IACUC/IBC/REC/ESCRO administrator
 - Researchers and staff
 - Institutional officials
 - Government representatives
 - Subject advocates
 - Ethicists
 - Policy makers
 - Pharmaceutical and biotechnology personnel
 - Attorneys
- <http://www.primr.org/>

Society of Clinical Data Management (SCDM)

- International organization (>2,400 members)
- Established 1994
- Founded to advance the discipline of clinical data management and support Clinical Data Management professionals
- Annual meeting and other educational offerings
- Developed professional standard for good clinical data management practices
- <http://www.scdm.org/>

Society of Clinical Research Associates (SoCRA), Inc.

- International organization (> 14,300 members)
- Established in 1991
- Provides educational programs and a forum for research professionals to exchange information
- Originally started for research professionals at a site
- Membership expanded to include monitors, data managers, and regulatory representatives from industry, academia, research centers, NIH and regulatory agencies
- <http://www.socra.org/>

Research Certification

- ACRP
 - Certified Clinical Research Associate (CCRA®)
 - Certified Clinical Research Coordinator (CCRC®)
 - Certified Physician Investigator (CPI®)
- SoCRA®
 - Certified Clinical Research Professional (CCRP®)
- PRIM & R
 - Certification for IRB Professionals (CIP®)
- SCDM
 - Certified Clinical Data Manager (CCDM®)

Regardless of Your Role: Be Your Own Best Advocate

- Protect your time & get organized
- Learn as much as you can about:
 - clinical trials
 - disease/condition
 - your particular interventions
 - your database/software programs
- Know how/where to get training & do it
- Join a professional organization & get involved
- Teach something new & you will learn
- Teach someone new & you will grow