

## Roles & Responsibilities of the Research Team



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## Introduction

All staff involved in clinical research must adhere to the regulations and understand the guidelines that govern clinical research. This module will provide an overview of the roles and responsibilities of the research team and support staff including those roles seen in the Center for Cancer Research: Investigator, Research Nurse, Data Manager, Clinical Research Nurse, and Pharmacist.

- At the conclusion of this module, you will be able to:
- Describe the role and responsibilities of the Investigator as described by OHRP, FDA, and ICH.
  - Describe the role and responsibilities of the Research Nurse
  - Describe the role and responsibilities of the Clinical Data Manager
  - Describe the role and responsibilities of the Clinical Research Nurse
  - Describe the role and responsibilities of the Pharmacist

## OHRP's Use of "Investigator"...

- OHRP interprets an "investigator" to be any individual who is involved in conducting human subjects research studies.
- Such involvement would include:
  - 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, and students, among others.
- With multiple investigators, one investigator is designated the "principal investigator" with overall responsibilities for the study.
- The next several pages will review OHRP's current thinking on the role of the investigator. To learn more, review [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

- FDA defines the responsibilities of the Investigator when conducting FDA regulated research.
- All Investigators should refer to 21 CFR Parts 11, 50, 54, 56, 312, and 812 for a more comprehensive listing of FDA's requirements.
- The Investigator is the one who has the overall responsibility for the conduct of the clinical trial and is often referred to as the PI in the protocol document as
- Other Investigators are referred to as Subinvestigators by the FDA or in the NIH community an Associate Investigator (AIs).

### 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 which appear on the next several slides



### 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 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 expect 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
- There is one Form 1572 per study
  - Exception: CTEP-sponsored trials have 1 form per investigator and must be updated at least annually. See their [website](#) for more information about Investigator registration for CTEP-sponsored trials.
- All copies of the Form 1572 are to be maintained in the regulatory binder.
- To learn more, review FDA's 2010 [Information Sheet Guidance for Sponsors, Clinical Investigators, and IRBs: Frequently Asked Questions—Statement of Investigator \(Form FDA 1572\)](#)

## 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.

## 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)).
- This guidance 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.

## International Conference on Harmonisation (ICH)

- International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use is an agreement between the European Union, Japan and the United States to harmonize different regional requirements for registration of pharmaceutical drug products
- Unique joint effort by regulators and associated pharmaceutical industry trade associations
- ICH guidelines have been adopted as law in several countries, but are only used as guidance for the U.S. Food and Drug Administration

## International Conference on Harmonisation (ICH) Guidances

- 4 major categories of standards are:
  - Quality guidelines
    - chemical and pharmaceutical Quality Assurance
  - Safety guidelines
    - in vitro and in vivo pre-clinical studies
  - Efficacy guidelines
    - E1-E2F: Clinical safety
    - E6: [Good Clinical Practice \(GCP\) Guidelines](#)
  - Multidisciplinary guidelines
    - cross-cutting topics that do not fit into one of the above categories

## E6: Good Clinical Practice (GCP) Guidelines

- This document:
  - Describes the responsibilities and expectations of all participants in the conduct of clinical trials, including investigators, monitors, sponsors and IRBs
  - Covers aspects of monitoring, reporting and archiving in clinical trials
  - Describes the essential documents that are to be maintained by the site and the sponsor
- The next several pages provide a summary of the Investigator's responsibilities as described in E6 Section 4

## 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

## 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

## 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 trial 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.

## 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

## **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

## **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

## **E6: Randomization Procedures and Unblinding**

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

## **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

## **...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

## **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

## E6: Safety Reporting

- The Investigator should:
  - Report all serious adverse events, including deaths, to sponsor and IRB/regulatory agency as per SOPs
- For more details, see Adverse Event module

## 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

## 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

## Sub-Investigator

- The definition of "sub-investigator" in FDA's official guidance, the "ICH E-6 Good Clinical Practice: Consolidated Guidance," states: "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)."
- It's important to recognize that any study staff who "make direct and significant contribution to the data" are considered "sub-investigators" which means they would also need to be listed in block #6 of the Form FDA 1572.

## NIH Associate Investigator

- **The NIH has 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. A lead associate investigator may be a physician, a dentist, a Ph.D., an RN, a member of the allied health professions, or a trainee.
  - **Associate Investigator(s) (AI)**
    - Individual(s), other than the PI, API, MAI or 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. There may be several AIs on a protocol.
    - *For CCR, note that contract data managers should not be included as Associate Investigators and should not be listed on the protocol Face Sheet.*

## Nurses

- Nurses involved in clinical research continue to serve as advocates for their patients. However, they now take on 2 additional advocate roles:
  - Subject advocate
  - Protocol advocate
- The trick is balancing the advocacy roles
- There are 2 main clinical research roles for nurses with a variety of names. At NIH they are referred to as:
  - Clinical Research Nurse (AKA: Staff Nurse)
  - Research Nurse Specialist (AKA: Clinical Trial Nurse, Research Nurse Coordinator)

## Nursing Roles

### Clinical Research Nurse (CRN)

Spends the majority of their time delivering direct care to research participants and their families

### Research Nurse Specialist

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

## Clinical Trials Nurse

- As defined in the [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. This is 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
- The next several pages will highlight these competencies.

## Protocol Compliance...

- Adheres to current regulations, guidance, and policies that affect research at the institutional, state, federal, and international levels.
- Complies with the processes and procedures required by different types of sponsors (e.g., private industry, National Cancer Institute Cancer Therapy Evaluation Program, investigator-initiated).
- Ensures security of research data and personal health information.
- Participates in discussions regarding feasibility of protocol implementation based on knowledge of institutional capabilities and limitations, therapy, or population of interest.
- Collaborates with the research team to implement procedures for maintaining patient study participation from enrollment through completion.

## ...Protocol Compliance

- Participates in providing timely, informative, and accurate communication to the IRB as required.
- Facilitates and participates in the preparation for and implementation of scheduled and unscheduled meetings with external and internal monitors and auditors (e.g., sponsors, FDA, IRB, QA).
- Ensures validity of research results by ensuring timely, accurate, and complete data documentation, reporting deviations, violations, and serious adverse events.
- Collaborates with principal investigator, pharmacy, and other appropriate personnel to ensure proper use of and accountability for experimental devices or drugs as indicated.

## Clinical Trials–Related Communication

- Ensures ongoing formal and informal communication regarding clinical trials with team members.
- Provides general clinical research as well as trial-specific information to research, clinical, and other organizational staff.
- Develops relationships with referring physicians, clinical staff, and ancillary departments to facilitate compliance with and accrual to clinical trials.
- Participates in study initiation meetings.
- Provides education related to clinical trials to patients and their significant others.
- Advocates for the safety and care of clinical trial patients as well as for the promotion and integrity of the clinical trial

## Informed Consent Process

- Ensures the initial and ongoing consent process is performed and documented in compliance with FDA, International Conference on Harmonization Good Clinical Practice (GCP), institutional, sponsor, IRB, and other applicable regulations, guidances, and policies.
- Participates in the education of clinical trial patients about their clinical trial and significant new information that is forthcoming during or after the conduct of the trial.
- Assesses for barriers to effective informed consent discussions and implements plans to overcome them.

## Management of Clinical Trial Patients...

- Collaborates with the investigator to ascertain study patient eligibility for a clinical trial, including documentation of criteria specified in the protocol.
- Ensures adherence to the protocol schedule of events and other requirements.
- Ensures scheduling of all procedures required to assess for adverse events and disease response to the study intervention.
- Ensures the successful completion of correlative components of the clinical trial (e.g., pharmacokinetic, pharmacoeconomic, and quality-of-life studies).
- Assesses patients for trial-related and non-trial-related symptoms and ensures evidence-based symptom management while maintaining trial compliance.
- In collaboration with the investigator, assesses patients for adverse events and then documents and reports these findings per the protocol, sponsor, IRB, FDA, and OBA regulations.

## ...Management of Clinical Trial Patients

- Utilizes adverse event assessment data and clinical judgment to determine if a dose-limiting toxicity has occurred or if any treatment schedule or drug dose modifications are necessary and communicates findings to the study team and sponsors.
- Evaluates disease response results and physical assessment data in conjunction with the principal investigator to determine response per the protocol.
- Supports and evaluates patient adherence to the protocol by utilizing various methods to assist with documentation, patient education, and study agent return.
- Identifies vulnerable patients who require increased nursing assessment and management in addition to the clinical trial requirements.

## Documentation...

- Complies with regulations, institutional policies, and sponsor requirements governing source data and documentation.
- Documents assessment, management, and evaluation in source documents for patients on clinical trials as appropriate to the protocol and role.
- Educates research and clinical team members regarding appropriate and accurate source documentation for participants in clinical trials.
- Ensures that relevant data from the source document are abstracted and recorded in the clinical trial case report forms and that every data point can be verified within the source document.

## ...Documentation

- Follows appropriate guidelines in making corrections to data entry in clinical records and case report forms as recommended by good clinical practices, standards, or institutional procedures.
- Ensures that all regulatory documents are processed and maintained per institution, IRB, and GCP.
- Demonstrates proficiency in the use of clinical and research-related computer programs.
  - *NOTE: This is a very important part of the role. Research Nurses may need to take classes to become more proficient with software products used in practice including Microsoft Word, Outlook and Excel.*

## Patient Recruitment

- Assists in implementation of recruitment plans to identify and assess individuals who might be eligible for clinical trials, taking into consideration the study entry criteria, required procedures, and other potential factors.
- Identifies and develops processes to overcome barriers to recruitment related to patient demographic factors, underserved populations, and healthcare system influences.
- Identifies institutional or community-based resources or groups that can assist in achieving recruitment goals

## Ethics

- Advocates for ethical care of clinical trial patients and the conduct of clinical trials in accordance with standards of nursing practice.
- Promotes ongoing compliance with key ethical concepts by the research team, including informed consent, documentation, respect for persons, beneficence, and justice.
- Ensures that members of vulnerable populations enrolled in clinical trials are identified and that their rights are addressed.
- Identifies and follows institutional procedures to report any falsification of data or scientific misconduct.

## Professional Development

- Participates in educational opportunities to increase knowledge about clinical trials, regulations and guidance, and the role of the research nurse.
- Seeks resources on an ongoing basis that provide oncology treatment and nursing practice updates, such as through professional mentoring and meetings, journals, and Web sites.

*NOTE: The research nurse role also incorporates an understanding about budgets and contracts which is not a focus for research nurse specialists at the NIH.*

## Clinical Data Manager (CDM)

- Individual responsible for some or all activities related to Clinical Data Management
- The CCR contracts some of the CDM activities as related to the CDM and database programmer roles.
- The next few pages will describe the roles of the CDM in the CCR.

## CDM Responsibilities...

- Collects source documents needed for data abstraction
- Abstracts research data from patient's medical record/source documents to the case report form (paper or electronic)
- Enters data into database(s)

## ...CDM Responsibilities

- Conducts self-audits to ensure data quality
- Manages protocol related data (i.e.: understanding what forms are still outstanding and what documentation is missing)
- Understands how CRFs are developed

## ...CDM Responsibilities

- Understands the various databases used and how to resolve problems associated with the different systems
- Provides periodic reports from database
- Assists in preparation for audits/monitoring visits

## Study Subject's Responsibilities

- The study subject has responsibilities as an integral member of clinical research.
- Their role needs to be reinforced as part of the informed consent process.
- Roles include:
  - Adhering to protocol specific schedule of events
  - Timely notification to the research staff including:
    - Adverse events
    - Changes in concomitant medications
    - Inability to comply with protocol criteria (e.g.: exclusionary meds, keeping appointments, patient diaries, etc.)
    - Change in status (e.g.: new phone #, adverse event, etc.) in a timely manner

## Clinical Research Nurse/Staff Nurse

- Provides direct patient care including treatment and patient education
- Adheres to protocol
- Documents all patient encounters in the medical record
- Collects specimen as per protocol
- Informs PI/Research Nurse Specialist of patient or protocol related issues/concerns

## Pharmacist

- Though the PI is ultimately accountable for drug accountability, this is 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 form (DARF)

Line No.	Date	Patient's Name	Patient's ID No.	Dose	Quantity Ordered/Received	Balance Forward/Balance	Manufacturer and Lot No.	Recorder's Name
1.								
2.								
3.								
4.								
5.								
6.								
7.								
8.								
9.								
10.								
11.								
12.								
13.								
14.								
15.								
16.								

## Example of a DARF

## Helpful Hints: Know Your Protocols

- Eligibility criteria
- Drug preparation & administration
- Schema, requirements, follow-up
  - PKs, research tests, restaging, drug return
- Dose limiting toxicity and/or dose modifications
- Reporting requirements
- Results (responses, toxicities)

## Helpful Hints: Know the Disease

- Etiology
- Epidemiology
- Signs and Symptoms
- Screening and Diagnosis
- Pathology Grading
- Disease Staging
- Treatment Options
  - What is standard therapy?
- Disease Trajectory
- Clinical Trials elsewhere for the same disease

## Regardless of Your Role: Be Your Own Best Advocate

- Protect your time & get organized
- Learn as much as you can about:
  - clinical trials
  - oncology
  - your particular drug(s)
  - 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

## Evaluation

Please complete the [evaluation form](#) and fax to Elizabeth Ness at 301-496-9020.



**For questions, please  
contact Elizabeth Ness  
301-451-2179  
ness@mail.nih.gov**