Chapter 33
Regulatory Considerations: The Clinical Research Coordinator

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The Clinical Research Coordinator, also known as Nurse Research Coordinator, Research Coordinator or Study Coordinator has a critical role in the conduct and success of a clinical trial. It has been said that the coordinator is the "heart and soul" [1] of a clinical trial. Although all responsibilities fall on the Principal Investigator (PI) [2], the Clinical Research Coordinator manages and oversees the day-to-day operation to ensure that all aspects of the clinical trial run smoothly from initiation to completion of the research study.

Professional Background

In 2007, the National Institutes of Health Clinical Center (NIHCC) issued the results of a role delineation project, *Building the Foundation for Clinical Research Nursing Domain of Practice for the Specialty of Clinical Research Nursing*. The document described the scope of research practice in nursing and framed it within two roles [3]: Clinical Research Nurses (CRN) and Research Nurse Coordinators (RNC). In certain settings those roles are not mutually exclusive. The CRN

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functions within a research unit, such as the NIHCC, research units in Clinical Translational Science Award sites, General Clinical Research Centers (GCRCs), or specialty care programs with a clinical research focus [3]. Their role is to provide and support all the clinically related activities of a study protocol. The RNC, however, is primarily responsible for study coordination and data management with a central focus on managing subject recruitment, integrity, and compliance with regulatory requirements and reporting [3]. The NIH Role Delineation Project defines five dimensions—distinct categories of activities—within the specialty practice of research nursing.

Clinical Practice

Direct nursing care is provided to participants in clinical research, with support to their families, and significant others. Care requirements are established by the scope of study, the clinical condition of the patient, and the requirements and clinical effects of research procedures and include functions such as history and physical exam, administration of study drugs, monitoring of effect and specimen collection, handling, and processing [3].

Study Management

The Research Coordinator ensures compliance with all steps of the protocol, accurate data collection and form completion. He/she maintains communication with the sponsor, IRB and different regulatory bodies [3].

Care Coordination and Continuity

Coordination of research activities without interfering with required clinical care and needs is an essential function of the clinical research coordinator, who should also achieve a relationship with referring and primary care providers [3]. Examples of activities under this dimension include the education of all caring for the patient on the study protocol, coordinating the scheduling of the study participants' visits, acting as the case manager for study participants, and answering participants' and providers' questions and concerns.

Human Subjects Protection

The Research Coordinator facilitates the informed participation of participants from diverse backgrounds in clinical research [3]. As an example, he/she makes the initial and ongoing informed consent process easier for the study participants by explaining the study protocol and answering questions and concerns. The Research Coordinator also works with the Principal Investigator and the rest of the team to address any potential ethical conflicts.

Contributing to the Science

The Research Coordinator is in a unique position to make observations during the conduct of a study that can lead to protocol amendments to minimize risks to participants, improve flow of the study or lead to new research ideas. In addition, the Research Coordinator will keep participants apprised of new findings resulting from a study and how it affects them.

Education and Training

Traditionally, the Research Coordinator's role was filled by a registered nurse. More recently others such as advanced practice nurses (NP), physician assistants (PA), and foreign-trained physicians who may choose not to obtain medical licensure in the United States have fulfilled the role of research coordinators and made significant contributions to the conduct of Clinical Trials. Historically Study Coordinators, Research Coordinators, and Nurse Research Coordinators have learned the duties of the position "on the job" being initially oriented and mentored by the Principal Investigator, by another site coordinator, or offsite study personnel [4]. Although this is still accepted today, the complexity and administrative requirements might require more formal training.

Training in clinical research is offered via programs leading to a Certificate, an Associate's Degree or a Bachelor Degree Program. These programs prepare the research candidate for entry-level positions in the field and provide them with certification. Other jobs such as Senior Research Coordinator, and Project Manager, may require a Master's Degree. Associate's Degree Programs in clinical research include general education courses along with specialized clinical research classes and may also include an internship [5, 6].

For a Registered Nurse or others with some medical experience, such as an NP, a PA, or a medical doctor from another country not certified in the United States, a certificate program may suffice. A solid foundation based on years of experience in nursing or the medical field makes the clinical research coordinator (CRC) an

excellent candidate. Others who have no medical foundation need to complete an Associate's Degree, Certificate Program that will cover basic courses in medical and research terminology and an introductory level course in clinical research. Example topics in a CRC educational program include clinical research management, drug safety, legal and regulatory compliance, clinical statistics, pharmacology for clinical trials and research ethics. Education in clinical research and clinical experience are required to work as a CRC. Although not mandatory, professional certification is available through the Society of Clinical Research Associates (SOCRA) and the Association for Clinical Research Professionals (ACRP) [7, 8].

Certification

The Clinical Research Professional certification (CRP) offer by SOCRA is available to members of the association who provide evidence of full-time employment in the field of research. The amount of experience the applicant is required to have is contingent upon the level of education and training completed. SOCRA has 3 "Categories" that would make a candidate eligible to take their certification exam:

Category 1. Minimum of two (2) years of fulltime employment as a clinical research professional in the past five years.
Category 2. Holds a degree in "Clinical Research" from an Associate, Undergraduate or Graduate Program and has completed a minimum of one year of full-time experience during the past two years as a Clinical Research professional.
Category 3. Holds an Undergraduate or Graduate Certificate in "Clinical Research" and holds an associate or bachelor degree in a science, health, pharmacy, or related field plus completed a minimum of one year of full-time experience during the past two years as a Clinical Research Professional.

The CRP is available for clinical research coordinators, principal investigators, researchers, and others working in clinical research [7].

A Clinical Research Coordinator certificate is offered by ACRP. To qualify for the ACRP certification, an applicant must provide evidence of an associate or bachelor degree or be a registered nurse (RN) and have a minimum of 3500 h hours of work experience. A high school diploma or experience as an LVN, LPN, medical assistant, or laboratory technician together with 4500 h Hours of related work experience will also meet the requirement. The ACRP offers other certifications, such as Clinical Research Associate (CRA) and Clinical Physician Investigator (CPI). Each certification requires that the applicant meets eligibility qualifications and pass an examination [8].

In addition to training and certifications all research staff engaged in human subject research must complete a Collaborative IRB Training Initiative (CITI) [9] or National Institutes of Health (NIH) course that meets the educational requirements for Human Subjects Protection and Good Clinical Practice [10]. These programs are

available online. Different research organizations also require other annual trainings on Privacy and Health Insurance Portability and Accountability Act of 1996 (HIPAA) regulations [11, 12].

Role in Clinical Research

The role of the CRC is complex; The CRC oversees and coordinates the daily activities of clinical research studies, works closely with the clinical multidisciplinary teams and investigators to ensure that all protocol required procedures and study visits occur according to protocol specified guidelines. The CRC works in many different settings including university or private hospitals, and government institutions such as the NIH, Veterans Administration, Centers for Disease Control and Prevention (CDC) and Department of Defense (DOD). They may also be employed in the pharmaceutical industry or private research sites. The CRC needs to have a wide range of skills and knowledge [13]. Prioritizing and decision-making skills are essential for this role. Excellent communication and interpersonal skills are a must since the CRC interfaces with clinicians, patients, sponsor, and the IRB. A range of computer skills are necessary as well. They generally manage participant enrollment and ensure compliance with the protocol and other applicable regulations, ascertaining that Clinical Trials are conducted according to governmental regulations and guidelines, International Conference on Harmonization (ICH) regulations [14], GCP guidelines, site's Standard Operations Procedures (SOPs), and other policies and procedures (Table 33.1).

Table 33.1 Functions of the clinical research coordinator

Prepares site initiation, monitoring, and close-out visits with the study sponsor
Attends investigator meetings
Facilitates the execution of the NDA[a]
Prepares and manages IRB and Ethics Committee documentation[b]
Participates in preparing the study budget and CTA[c]
Participates in the development and execution of the CRADA[d]
Reads and implements protocols, informed consent forms, investigator's brochures, and other study guidelines
Maintains participant data in CRF/eCRF
Trains new personnel/medical staff in protocol implementation and adherence
Aids in the development and implementation of a recruitment strategy
Screens and enrolls subjects
Maintains a recruitment log[e]
Serves as a liaison between study subjects and the Principal Investigator

(continued)

Table 33.1 (continued)

Obtains, in collaboration with the Principal Investigator, the ICF and maintains these forms in regulatory binders
Develops and implements a retention plan for subjects in the study
Monitors for early subject withdrawal
Ensures Principal Investigator performs protocol specific tasks
Randomizes subjects and assigns study numbers
Informs subject and dispenses study medication(s) or device(s)
Manages study finances and subject stipends
Records/Reports all (serious) adverse events to the Principal Investigator, study sponsor and IRB
Documents and explains any premature unblinding of the study drug or investigational product
Manages the receipt, distribution, retrieval and return of all clinical supplies
Ensures that Principal Investigator reviews and signs required study documents
Communicates with and updates the study sponsor regarding study activities
Responds to data queries
Prepares a records retention and storage plan[f]

Abbreviations: *NDA* Non-disclosure Agreement, *IRB* Institutional Review Board, *CTA* Clinical Trial Agreement, *CRADA* Clinical Cooperative Research and Development Agreement, *CRF* Case Report Form, *eCRF* Electronic Case Report Form, *ICF* Informed Consent Form

[a]A legal contract between at least two parties that outlines confidential material, knowledge, or information that the parties wish to share with one another for certain purposes, but wish to restrict access to or by third parties

[b]Original submission, annual renewal, protocol amendments or deviations, adverse events, data safety monitoring board reports, visit reports, participant recruitment tools, and other reports provided by the study sponsor

[c]Include terms for indemnification, confidentiality, publication, intellectual property, insurance, data safety and monitoring boards, subject injury, governing law, and termination clauses [15]

[d]An agreement between a government agency and a private company or university to work together on research and development [16]. In study sites that are part of the Federal Government such as the Veterans Administration

[e]Lists subjects who were contacted for enrollment and reason subject either declined to participate, met exclusion criteria or failed to meet inclusion criteria

[f]Must follow research site's policies and procedures and be in accordance with requirements for the protection of human subjects in research (45CFR 46.115) [17] and the FDA-device policy [18]

Role in Human Subjects Protection

Clinical Trials are critical for enhancing standards of patient care and patient satisfaction with healthcare. The Clinical Research Coordinator is in a unique position to be a patient advocate and study advocate when conducting Clinical Trials. One of the most vital roles of the Study Nurse Coordinator is to ensure the safety and welfare of study subjects. On virtue of his/her education, background and clinical skills, the CRC is able to prioritize the patient's needs and best interests as well as protect their welfare during the trial. Subject advocacy promotes an informed decision to participate in research [19]. By carrying out the objectives of the study protocol, the CRC is also able to advocate for the study to ensure that all steps of

the protocol are followed and that scientific goals are met. Because of their central position, holistic perspectives and their commitment to balancing the three advocacies, CRCs are uniquely positioned to advance the goals of human subjects protection and advancement of knowledge.

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