The Essential Role of the Clinical Research Nurse (CRN)

Rebecca Deal Poston
Christine R. Buescher

In an age of increasing focus on expanding the opportunity of clinical research trial participation to broader patient populations, the clinical research nurse (CRN) has become an essential member of the clinical research team. The CRN is responsible for many roles and aspects of clinical trial management. Clarification of these roles and responsibilities will be provided in this article.

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The role of the clinical research nurse (CRN) is an exciting one for nurses who are interested in expanding their knowledge and enhancing their clinical skill set to make a difference on the front lines of patient care. As a crucial member of the multidisciplinary clinical research team, the CRN has the privilege of participating in a process that affords a unique opportunity to offer novel treatment approaches to patients who may have otherwise reached a dead end in their treatment course. The CRN is able to navigate new pathways for disease management with the clinical research subject. Through collaboration with other patient care services (such as pharmacy, radiology, and laboratory), the CRN is able to integrate knowledge and skills to provide comprehensive care within the confines of the clinical research trial.

The multicenter, randomized, double-blind, placebo-controlled clinical trial is the gold standard for clinical pharmaceutical and medical device research. The protocol is the map that directs how the trial is conducted. In addition to developing the investigational product and protocols to evaluate it, industry sponsors recruit investigators and sites across the country, and often, internationally to manage the clinical trial. Sponsors must maintain control of clinical research activities to assure quality data for marketing evaluation and ultimate approval. The sponsor must identify knowledgeable and diligent investigators who have an adequate patient population from which to enroll eligible subjects, as well as staff qualified to conduct the trial. At the clinical site, the research team consists of investigators, clinical research coordinators, laboratory personnel, pharmacists, and data entry and clerical staff. This article will address the role of the nurse as a clinical research coordinator (CRC) or CRN.

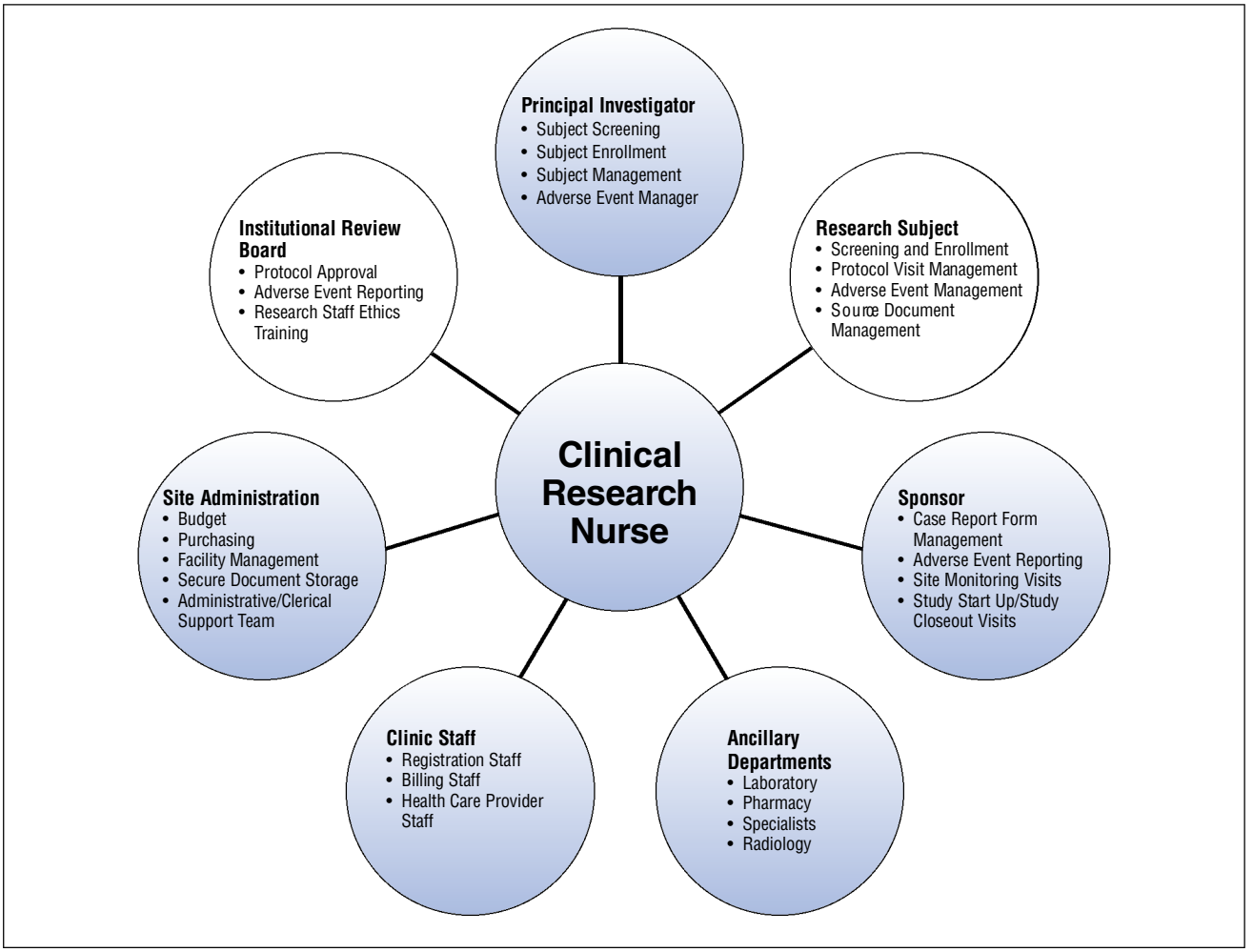
The role of the CRN, who may be an LPN, RN, or an RN with an advanced degree, has rapidly become essential to the day-to-day management of clinical research. Although the principal investigator (PI) has ultimate responsibility for all study activities at the site, the CRN coordinates the day-to-day management of the trial. The integrated efforts of the CRN (or CRC) and the PI, as well as the collegial relationship between the CRN and the PI, are essential to the implementation and management of the clinical trial protocol and its ultimate success (Pelke & Easa, 1997). The CRN is employed by the site, which may be a hospital, university setting, private medical practice, or private research facility. The responsibilities of this role are very time consuming, and it is beneficial for this nurse to dedicate his or her time to the clinical trials while other nurses handle the usual clinical duties. Most often, the CRN is hired specifically to assist in the conduct of clinical trials, but because nurses with extensive clinical trial experience are few, some on-the-job training is usually required. This training must be provided by someone experienced in clinical trials, either the PI or an experienced CRC.

This article serves to articulate the roles and responsibilities of the CRN involved in clinical research sponsored by pharma-

Rebecca Deal Poston, MSN, RN, CPNP, *is a Lecturer, Old Dominion University, School of Nursing, Norfolk, VA.*

Christine R. Buescher, BS, CCRC, *is a Consultant, Virginia Beach, VA.*

Figure 1.
Clinical Research Nurses' Primary Responsibilities and Key Team Members for Clinical Trial Management



ceutical and device companies (see Figure 1). Although these roles and responsibilities may be similar in an investigator-initiated trial or a federally sponsored research trial, the arena of interest for the purposes of this article will remain in clinical research trials initiated and sponsored by industry.

Step 1: Protocol Assessment And Review

The protocol (or frequently, a series of protocols for a compound) is written by the sponsor and approved for implementation by the U.S. Food and Drug Administration (FDA). The objectives, population, methods, and safety measures have usually been established by the time the site is notified of the study. The sponsor or contracted research organization (CRO) contacts sites with whom they may have had previous collaboration, were referred by other sites, or may be listed in an online database, such as Center Watch (www.centerwatch.com). Sites can list their information with Center Watch, indicating the type of trials in which they are interested, hoping to attract sponsors' attention.

The sponsor or CRO introduces the study, determines the site's interest, and preliminarily discusses capabilities. Although the sponsor is responsible for the development of the protocol, the CRN's role at the initial stage of protocol assessment may include a review of a proposed protocol for implementation at the site. With in-depth knowledge of the patient population, disease process, and requirements for systems integration of patient care, the CRN has a unique and valuable perspective when reviewing a protocol for acceptance. It is important to evaluate each protocol for feasibility in each specific clinical site. As the CRN reviews the protocol, it is important to evaluate the protocol on the following points:

- Do we have the patient population to support the recruitment plan?
- Does this protocol apply to our specific patient population in a way that will be beneficial?

- Do we have the staffing to support the management of this clinical trial?
- What members of the multidisciplinary team will be necessary to successfully complete the trial (such as pharmacy, radiology, laboratory services, speech pathology, psychology)?
- Is the recruitment timeline reasonable for our current workload?
- Is the protocol ethical as written?
- What is the risk/benefit to the subject and his or her family?

The CRN will discuss these issues with the PI, whose patient population, or referrals to the site, will serve as the potential subject pool. It is the experience of these authors that the CRN is often more realistic about the protocol feasibility at his or her site; therefore, CRN input during the assessment is critical. When answering these key questions, the CRN uses a level of knowledge and experience that provides realistic grounding to the discussion. Evaluation of the protocol on these points is crucial to the protection of future subjects and the success of the clinical research trial.

Protocol review conversations should be collaborative discussions between all members of the clinical research team, including the CRN, the PI, and appropriate ancillary support team members. It is important to ensure a good match between the clinical site and the protocol, and this valuable discussion can serve to eliminate unrealistic or undesirable protocols from consideration. Thus, the insight and experiences of the CRN can play an integral role in ensuring that the potential site is a match for the protocols being considered.

Step 2: Site Qualification Visit

Once the clinical research team has determined they would like to participate in the trial sponsored by a pharmaceutical or device company, the sponsor may elect to complete a site qualification visit. This visit may be facilitated by either a representative from the sponsor study team or by contracted research organization (CRO) staff. This visit is to document that the site has all requisite tools to successfully complete the clinical trial. This checklist often includes many of the same items evaluated by the site research team during the protocol assessment process. The sponsor will want to know if the site can recruit a reasonable number of qualified subjects to participate and complete the clinical trial, and if the site has all of the ancillary support services in place for successful study completion. This may involve an inspection of laboratory services and subject specimen storage facilities. This visit may include a review of site-specific standard operating procedures for topics as varied as subject document storage and protection to spirometry equipment calibration procedures. The success of such a visit qualifies the site for participation. The CRN is responsible for integrating and ensuring that all required research tools are present during this visit.

Step 3: Regulatory Submission

Each clinical trial must receive approval from all appropriate regulatory bodies for each clinical site prior to the implementation of the study/protocol. Typically, the document submission and receipt of approval is a lengthy and time-consuming process managed by either the CRN or a regulatory specialist. In an academic institution, the regulatory body responsible for the protection of human subjects is the Institutional Review Board (IRB). In a private practice clinical site, an affiliated academic institution's IRB or a central IRB may be utilized. Central or commercial IRBs work as fee-for-service businesses and are available to sites that do not have a local affiliated IRB or to sponsors. A sponsor can hire a central IRB to serve as the IRB of record for all sites conducting the protocol. Both types of IRBs are governed by federal regulations set forth by the U.S. Department of Health and Human Services Office of Human Research Protections (45 CFR 46).

The regulatory submission typically includes but is not limited to submission of the protocol, advertising, the drafted informed consent form, educational materials, any documents that will be used to collect data, and a plan for the protection of the privacy of any data collected or obtained during the course of the clinical trial. Members of the clinical research team must submit their credentials and verification of human subject protection training during this regulatory process.

Ultimately, the PI is responsible for all aspects of the clinical trial, but the CRN may assume some level of delegated responsibility for the regulatory process. This may include but is not limited to preparing documents for submission to the IRB, tracking approval from the IRB, submitting data periodically to the IRB for review and approval of trial continuation, and reporting any adverse events that may occur within the confines of the clinical trial. Depending on the policies of the research site, additional approval may be required from the hospital or other clinical entity prior to study initiation. This additional approval provides oversight for the study and provides administrators with knowledge about all research being conducted at their institution, as well as an assessment of the trial's impact on the site's clinical, pharmacy, and laboratory staff. It is essential that compliance with all local, state, and federal guidelines for the study of human subjects is followed, and the CRN may be delegated to track this documentation throughout the duration of the clinical trial.

Step 4: Investigator Meeting

In addition to IRBs, multisite clinical trials are subject to

strict regulation by a federal agency, the FDA. The FDA requires documentation of all participating PIs' or sub-investigators' standardized training on the protocol and its implementation. In past years, this process involved an Investigator Meeting held in a centralized location conducted by the study sponsor. It is customary for the CRN to attend this meeting. The investigator meeting can be a very helpful orientation to the clinical trial protocol and the practicalities of implementing the protocol at each individual site. This forum for training and collegial discussion often focuses on practical application and concerns that may require protocol adjustment. Vendors (such as centralized laboratory companies) that will be used to support the protocol are often available to answer questions and provide training. Financial constraints have curtailed many of these meetings, replacing them with Web-based seminars and on-site training by the CRO staff or a representative from the pharmaceutical trial team.

Step 5: Budget Management

Budget management is typically the responsibility of the CRN or a financial staff member. Although development of the budget can be done simultaneously with the regulatory submission, it should not be finalized until after the investigator's meeting, where unanticipated details affecting costs may emerge.

Although the sponsor usually provides basic budget figures, it is up to the site staff to determine the true cost of conducting the trial in their setting. It is important to ensure that all costs are covered; this includes personnel costs, equipment and supply costs, and administrative costs. Personnel costs must incorporate the PI's and CRN's time (salary and fringe benefits), pharmacist's charges, and both the technical and professional charges for the completion of study diagnostics (such as ECG, radiology). Equipment and supply costs may include any associated costs required to implement the study protocol, such as clinical and pharmacy supplies (including IV placement supplies for a procedure, drugs for sedation). Administrative costs may include subject compensation and travel expenses (if applicable), telephone and fax charges, postage and shipping, copying costs, and record storage after study completion.

When budgeting the CRN's time, consider preparation, recruiting, subject visits, documentation, communication with subjects, monitors, and primary care providers (PCPs) monitoring visits, and closing out activities. Time and effort of other involved staff members should be included. Start-up costs should be included in the site's budget as a non-refundable, up-front payment; they should include time and effort of all personnel involved in the initial activities, IRB fees, and advertising expenses.

It is important to understand the payment schedule defined in the contract; it should describe the initial start-up payment and criteria for subsequent payments. Although some sponsors have an automatic payment system that may be based on the number of subjects enrolled or specified time-frames, many require the site to send invoices for payment. The CRN may need to establish a tickler system to simplify this process. The contract should include details about the final payment, which usually includes holding a percentage of the total budget until the study is completed and all queries are resolved at *all* sites. Negotiating the payment schedule can be critical. To minimize potential financial loss, the clinical trial agreement (contract) must not be signed until the budget has been agreed upon by the site and the sponsor.

The CRN will need to work with patient registration staff at the clinical site to establish research accounts that will monitor research income and expenses, and to ensure proper payment for research tests and procedures. It is critical that tests and procedures are billed correctly, and that no double billing occurs. This will require the understanding of proper procedures by the clinic billing staff and may require extensive communication with outside entities used for specialized testing. The CRN will need to be very clear with the registration and billing staff regarding any procedures that are to be billed to the subject as standard care, payable by the subject or the subject's insurance, or any research procedures that are payable by the study sponsor through the research account. Federal regulations and IRBs prohibit billing the subject for investigational drugs except in very special circumstances (21CFR312. 7[d]) (FDA, 2009d). Regulations allow sponsors to charge for an investigational device; however, the charge should not exceed an amount necessary to recover the costs of manufacture, research, development, and handling of the investigational device (21 CFR 812.7[b]) (FDA, 2009c).

It is important to remember that if the protocol is revised during the study or the number of local subjects is increased, a budget amendment may be necessary to cover any increased costs associated with a protocol amendment or increased payment from the sponsor. The sponsor should cover the entire cost of conducting the study; budget management is a critical component for the success of a research endeavors.

Step 6: Clinical Trial Document Preparation

Once a clinical trial protocol has received approval, the development of a portfolio of clinical trial documents occurs. Developing these documents is typically the role and responsibility of the CRN. This document preparation step may include creating:

- Checklists for inclusion and exclusion criteria.
- Source documents: the recording of all subject interactions (such as protocol visits, laboratory reports, diaries, questionnaires, telephone, and e-mail communications, and adverse event reports). Source document worksheets may be created by the CRN or provided by the sponsor.
- Ongoing history forms for documentation during the clinical trial.
- Logs for patient refusal and patient participation.
- Logs for delegated clinical trial research staff with associated responsibilities.
- Any other tools that may be helpful in organizing the vast collection of data essential in the management of a clinical trial.

Each subject will have a clinical trial research chart separate from the medical record. The research chart will contain:

- The original signed informed consent form.
- Demographic information.
- Source documents, the recording of all subject interactions (such as protocol visits, laboratory reports, diaries, questionnaires, telephone communications, e-mail communications, adverse event reports), whether created by the CRN or provided by the sponsor.

A helpful tool for the CRN to develop is the clinical trial or study manual. Sponsors may provide various documents and tools that can be included in this manual; the CRN should review documents provided by the sponsor and supplement with others that will be useful. A reference manual kept in a centralized location should include 1) the most recent version of the approved protocol and informed consent, 2) a log of all clinical trials research staff with outlined delegated roles and responsibilities, and 3) any relevant source documentation forms. The development of this manual is especially important because it helps organize the clinical trial process and may serve to illuminate systems issues that require attention in the management of a clinical trial. A study flow chart that includes the required documentation at each stage of the study may also be helpful. The development of this type of tool will help clarify each specific protocol requirement and the necessary steps for the CRN to complete at each study visit.

Another helpful tool is a pocket-sized laminated card with study-specific inclusion and exclusion criteria noted. This is a memory aid to distribute to PIs and sub-investigators so they have an easy reference to utilize in clinic while considering patients for inclusion in the clinical research trial. Inclusion and exclusion criteria are often very specific and may have intricate details not readily memorized by clinical research staff. A pocket guide to these specific criteria for inclusion will be useful at the study start and throughout the duration of the study, especially when the site is conducting more than one trial.

Step 7: Site Initiation Visit

Once IRB approval is complete and all financial documents have been executed between the study site and the pharmaceutical or device sponsor, a site initiation visit can occur. The regulatory approvals will already have been forwarded to the sponsor, but the CRN must retain a copy. The CRN will provide any site-developed study document preparation for the study sponsor representative or CRO staff to review. This visit also serves as refresher training on the current protocol version for all involved research staff, most importantly the PI and CRN.

The CRN will be the liaison to the sponsor representative to ensure that all study supplies have been received and logged by the study site, including any investigational products. Each site has specific guidelines for appropriate management and documentation of study supplies, and the CRN is ultimately responsible for overseeing this aspect of the clinical trial.

Step 8: Ancillary Staff Education (In-Service)

At the beginning of a clinical trial, it is important to provide an educational presentation to all health care providers who may contribute to certain aspects of the clinical trial. These may include registration staff, clinic nursing personnel, sub-investigators, business managers, and radiology, pharmacy, and laboratory staff members. The PI should attend to communicate the importance of the study to the clinic staff and provide additional input. This educational forum should provide a brief introduction to the clinical trial protocol and eligibility requirements for subject inclusion. Nursing staff may be instrumental in identifying appropriate candidates for clinical trial participation. The support of all health care personnel is vital to the success of the trial. Various aspects of clinical trial management, such as pharmacy support, patient billing, and patient registration, are often neglected in study start-up activities, yet their informed participation in the clinical trials process is crucial to a successful and smooth clinical trial process.

Without a cadre of qualified research participants, the clinical trial will not succeed. It is vital to include other members of the research team in this initial introduction to the protocol. It is important to remember that the clinical trial is a team effort, and all members of the team must understand their own role as well as the role of others to succeed. The CRN is responsible for the overall coordination of the clinical research team.

Step 9: Patient Recruitment and Retention

Once the CRN has organized all documents and staff in antici-

pation of the start of the clinical trial, the focus shifts to patient recruitment. Using inclusion and exclusion criteria worksheets, potential patients are identified. Once identified, a number of approaches can be helpful when evaluating patients for study inclusion. In these authors' experience, the most successful approach for identifying eligible patients has been to screen all charts for patients scheduled to see the PI or sub-investigator in one-week intervals. Physicians and staff are allowed to screen their own patients for research, but this should be cleared with the IRB approving the trial. HIPAA regulations regarding work in preparation for research come into play.

The patient chart can be screened for basic inclusion and exclusion criteria by the site's staff, most often the CRN. Nurses should check with the IRB or privacy officer to verify that the processes are HIPAA-compliant. Once a patient's chart has been reviewed, and it appears that the patient will meet eligibility criteria for the study, a simple flyer, including a brief description of the study and inclusion/exclusion criteria, should be placed in the patient's chart to remind the PI and/or sub-investigator to solicit participation. It is important to remember that ethical research involves providing the opportunity for participation to all patients who are eligible. Equitable access to research is a fundamental cornerstone to ethical research practices.

If the patient meets eligibility criteria, he or she is approached in a private area of the clinic and provided information to review about the clinical trial. In these authors' experience, the most successful recruiting approach is to have the PI or sub-investigator initiate and solicit participation from potential subjects. There is an inherent level of trust and a well-developed therapeutic relationship between patient and provider that is essential when discussing clinical trial participation. However, the investigator must make it clear to the patient that participation in the trial is participation in research and is not simply an alternative treatment so as to avoid the pitfall of therapeutic misconception. This initial discussion begins the first essential step of the process of informed consent. Once the patient has been approached by the PI or sub-investigator, the CRN may be called in to discuss trial participation in detail with the patient. Effective retention begins with effective recruitment. Education of qualified potential research subjects will serve to improve overall retention for the duration of the trial. Study completion according to protocol equals evaluable data. Without appropriate screening and planning on the part of the CRN, these goals cannot be met (Luepker, 2003).

Step 10: Informed Consent

A valid informed consent is required for participation in any clinical research trial (45 CFR 46) (U.S. Department of Health and Human Services [DHHS], 2005). It is important to remember that the requirement for informed consent is not merely met by completing a signed informed consent form; it is a process that requires participation from the clinical research staff and the subject, as well as his or her family or support system. The informed consent process must be an ongoing conversation that begins at study introduction and continues throughout the duration of the subject's participation. CRNs may be delegated to perform this integral process by the PI and are often tasked with ensuring an ethical informed consent process throughout the duration of the clinical trial. The CRN must be a patient advocate and may bring issues related to eligibility, informed consent, and continued participation to the attention of the PI.

Formal training on appropriate procedures involved in informed consent is provided and/or required by the regulatory bodies that oversee clinical research in each specific clinical site. An example of a clinical research training program for research staff participating in the research of human subjects is the Collaborative Institutional Training Initiative (CITI) developed by the University of Miami and the Fred Hutchinson Cancer Research Center. This training provides a brief overview of ethical and regulatory aspects of the research of human subjects. The National Cancer Institute at the National Institutes of Health also provides a shorter training program. The IRB used for a site's trials may specify which program they accept. Informed consent is an area that often requires frequent continuing education, and it is the responsibility of the CRN to pursue this continuing education to ensure an ethical process.

Step 11: Subject Management

Throughout the clinical trial, the CRN is responsible for the management of the protocol, but most importantly, for the management of the research subject. Appropriate and careful attention to both the details of the protocol and the details of the research subject's progression throughout the clinical trial is crucial. The CRN becomes the "lifeline" or central mode of communication between the research subject and the clinical research staff. Without close and careful attention to the intricacies of the research subject's trial experience, successful implementation of the clinical trial protocol cannot occur.

One of the first activities that occurs after the informed consent is obtained is the assignment of the subject number. Throughout the length of the trial, this number and the subject's initials are the only identifiers provided to the sponsor. The subject number and initials are entered on any hard copy (diaries, CRFs) and electronic documents (eCRFs, emails) used to collect and report subjects' clinical data.

Research subjects are often asked to keep symptom and medication adherence diaries, as well as report any change in medical management to the study staff. The CRN is responsible not only for collecting and documenting these data, but also integrating the information provided by the subject with a foundational knowledge of the disease process and appropriate approaches to symptom management. An open dialogue of communication between the research subject and the CRN creates a forum for integrated care throughout the clinical trial process. The CRN is responsible for communicating any changes in subjects' symptoms or medical care to the responsible parties involved in the clinical trial, including the PI, sub-investigator, the IRB, and the study sponsor.

Step 12: Data Collection and Management

The goal of a clinical trial is to effectively collect data that will aid in bringing a new drug or device to market by securing licensure and thereby making the product available to potentially millions of individuals who would benefit from its use. As previously mentioned, the product of efficient and successful clinical trial management is thorough, careful documentation that produces reliable and retrievable data (Headlee, 2004). The primary point of data collection occurs between the CRN and the research subject. The CRN is responsible for collecting all protocol-specific data and recording such data in an organized and federally mandated manner. The responsibility of the investigator, as defined by the FDA's Code of Federal Regulations, is to

> *...prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records, including progress notes of the physician, the individual's hospital chart, and the nurses' notes. The case history for each individual shall document that informed consent was obtained prior to participation in the study* (FDA, 2009a).

The CRN carries the key responsibility of organizing the subject study chart and must have up-to-date and detailed knowledge of all study documents, including valid original signed informed consent, documentation of inclusion/exclusion criteria qualification, previous qualifying medical history, ongoing medical history, adverse event documentation, source documents, and case report forms.

Advancing technology has allowed for the case report form to evolve from a standard duplicate paper document to an electronic case report form (eCRF), which is more commonly utilized. The case report form is the domain of the CRN; it is crucial documentation of all subject-specific, relevant, protocol-required data. The FDA has provided CRNs with regulations for protecting research data and the use of this electronic data capture mechanism (21 CFR Part 11) (FDA, 2009b). These regulations outline the necessity of all users having passwords and following security precautions. All changes in data are tracked, and users making changes to original source documentation are clearly identified to provide a reliable chain of events in an electronic format.

Step 13: Ongoing Site Monitoring And Sponsor Communication

The sponsor of the clinical research trial will schedule periodic site-monitoring visits to review all collected patient data points with the CRN and the PI. Each data point collected in the source document must match each data point reported in the case report form or the electronic case report form. Periodic review of subject clinical trial records by the sponsoring pharmaceutical company or their representative (CRO staff) is implemented to insure accurate reporting of clinical trial data. Preparation and management of these site-monitoring visits fall within the domain of the CRN. As mentioned previously, the subject study chart and all collected data and source documentation is the domain and delegated responsibility of the CRN. Although research study records are maintained in the research area, clinic charts or hospital medical records may need to be requisitioned for the monitor's review.

As the clinical trial sponsor staff or CRO staff reviews individual subject charts, queries or questions regarding data points may arise. The query is the common form of data clarification between sponsor and clinical trial site staff (CRN). If there is a discrepancy between data points reported to the clinical trial sponsor and the data collected in the subject source documents at the clinical trial site, the query will serve as a mechanism to resolve this discrepancy. It is the responsibility of the CRN to address all queries in a timely manner and resolve any data issues highlighted during the site-monitoring visit.

In addition to monitoring trial-specific subject data points, the clinical trial sponsor or CRO staff will monitor all regulatory documentation throughout the trial. This will include all IRB correspondence, protocol amendments, reporting of adverse events, continuing review of the protocol by the IRB, and clinical trial staff licensure. The CRN is responsible for keeping tidy and organized records of all regulatory documents. If any missing documents are identified during the site monitoring visit, it is the responsibility of the CRN to address these action items in an efficient manner.

Step 14: Study Close Out/Reconciliation

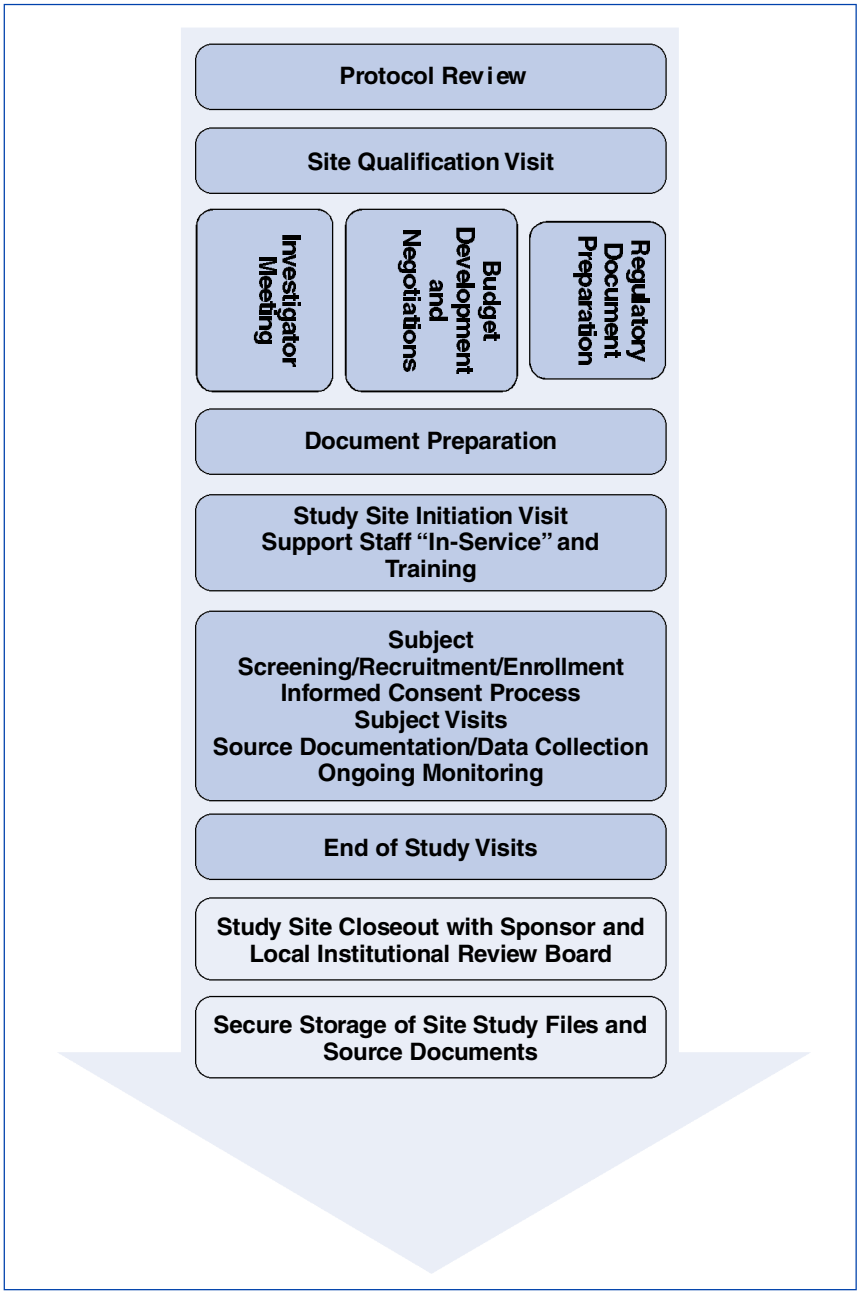
At the conclusion of the clinical trial, the CRN is responsible for the study closeout procedures. These procedures and the timing may vary according to clinical trial sponsor and study methodology. The timeline for study closeout typically coincides with the closure of all open data queries following the last visit by the last patient. Final reconciliation of all open data queries must be completed by the CRN and approved by the PI. In an age of electronic case report forms, the clinical trial sponsor may provide an electronic record of all clinical trial data collected by the specific site for the PI and CRN to review and approve as accurate and complete.

Following the closure of all data collection, the study sponsor may schedule a closeout visit to complete any final monitoring requirements and inventory and return any study-specific equipment or supplies. The CRN is typically responsible for tracking and documenting use of all study-specific equipment and supplies, and the final inventory will occur at the closeout visit with the study sponsor. The CRN or regulatory specialist must notify the IRB of study closeout.

Following study closeout at the site by the clinical trial sponsor, all site specific source documentation and regulatory documents must be retained and stored by the study site per Federal Regulations. According to the Federal Code of Regulations 21 Section 312.62(c):

> *...an investigator shall retain records required to be maintained under this part for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified" (FDA, 2009a).*

Figure 2.
Clinical Trials Timeline by Clinical Research Nurse Tasks



Essential clinical trial steps and stages are outlined in Figure 2.

CRN: Certification and Professional Development

The responsibilities of the CRN can be achieved by nurses with a wide variety of backgrounds. The key components to success in this role include a high level of organization, attention to detail, and a passion for patient advocacy. The relative consistency of schedule and lack of rotating, night, weekend, or holiday shifts make this role attractive for many nurses looking for a new arena to develop their skills.

The Association of Clinical Research Professionals (ACRP) (www.acrpnet.org) offers a certification examination for the clinical research coordinator, including the CRN. The certification requires candidates to sit for an examination that provides the

credentials of Certified Clinical Research Coordinator (CRCC). This certification examination validates the unique skill set and experience required of a CRN and is recognized in the global clinical research arena as a verification of clinical site staff qualification.

The Society of Clinical Research Associates (SoCRA) (www.SoCRA.org) also offers a certification examination for which the CRN may be eligible. This certification program verifies expertise in the development, management, and administration of clinical trials. Following successful completion of this certification process, the CRN may be identified as a Certified Clinical Research Professional (CCRP).

CRN: Ethical Conflicts in Research Administration

In addition to the CRN's responsibility to the patient as advocate and caretaker, he or she has an obligation to the PI and clinical trial sponsor to follow the prescribed protocol. In the realm of clinical research, the CRN truly embodies the "catch all" role for the management of the administration of the clinical trial, as well as the management and protection of the human research subject.

Patient advocacy is at the core of a nurse's practice ethos. In Provision 1 of the Code of Ethics for Nurses, the American Nurses Association (ANA) (2008) states that nurses strive to "practice with compassion and respect for the inherent dignity, worth, and uniqueness of every individual, unrestricted by considerations of social or economic status, personal attributes, or the nature of health problems" (p. 143). Provision 2 outlines that nurses' "primary commitment is to the patient, whether an individual, family, group, or community" (ANA, 2008, p. 143). There may be a situation where the CRN feels that the primary commitment to the subject is threatened. Potential threats related to the protocol design, pressures from the industry sponsor, and/or the PI's conflicting interest may arise. It is important for the CRN to maintain the primary commitment to the subject and serve as an advocate. The clinical trial sponsor and/or the PI may have conflicting interests in the application of the protocol. The treatment offered in the control group may not be consistent with the current evidence-based practice, or certain patient groups may not be eligible under study protocol for all available treatments. If the PI or CRN believes the protocol design or use of an inappropriate comparator (placebo or active drug to which the investigational product is being compared) is unethical, participation should be declined. The CRN has a voice to offer valid arguments for protecting his or her commitment to the patient, and in the case of clinical research, the patient subject.

Maintaining balance in commitment to all involved stakeholders in clinical research is difficult and successfully managed by the experienced CRN. While nurses must strive to protect the health, safety, and rights of the patient first (ANA, 2008), nurses must also be able to reasonably juggle all other commitments to other stakeholders in the clinical trials process (for example, PI, study sponsor, FDA).

Does the CRC Need to be a Registered Nurse?

The unique code of ethics that governs nurses as developed by the ANA (2008) describes the duties and ethical guidelines that govern the patient-nurse interaction. This code creates a foundation for relationships between patients and nurses that should also be applied in the realm of the clinical trial where the patient becomes the research subject. In an age of increasing staff shortages in all aspects of health care, the role of the CRC has been staffed with non-nurse applicants. It is the opinion of these authors that the intricacies of both pharmacology and pathophysiologic knowledge, which provide critical foundational knowledge for managing clinical research trials, demand the research coordinator to be a registered nurse. The involvement of a CRN in clinical trials has shown an increased rate of patient enrollment and has an overall positive impact on the completion of the clinical trial in a timely manner (Isaacman & Reynolds, 1996). Spilsbury et al. (2008) highlight that the CRN has an important role in improving data quality and trial protocol compliance. The benefit of an experienced nurse with knowledge of the specific population under study is evidenced by the day-to-day management of the clinical trial patient population in an efficient and safe manner.

Conclusion

The role of the CRN can be fulfilling and provide opportunities for knowledge development and skill acquisition in an arena that is ever changing. At the core of the mission of the research of human subjects is the desire to gain knowledge that facilitates the development and approval of new treatment modalities for patient care. The CRN role is critical to this process in ways that at first may seem subtle, but after in-depth examination, reveal that the CRN is at the fulcrum of clinical trials work.

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