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Clinical Trials & the Role of the Oncology Clinical Trials Nurse

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Abstract

Clinical trials will continue to be paramount to improving human health. New trial designs and informed consent issues are emerging as a result of genomic profiling and the development of molecularly targeted agents. Many groups and individuals are responsible for ensuring the protection of research participants and the quality of the data produced. The specialty role of the Clinical Trials Nurse (CTN) is critical to the implementation of clinical trials. Oncology CTNs have established competencies that can help guide their practice; yet, not all oncology CTNs are supervised by a nurse. Using the process of engagement, one organization has successfully restructured the oncology CTNs under a nurse-supervised model.

Keywords

Clinical trials; oncology trial design; Clinical trials nurse; Clinical Trials Nurse; Research Nurse competencies; Research Nursing Office

INTRODUCTION

Today's standard of care was yesterday's clinical trial. Oncology clinical trials have been and will continue to be the cornerstone for improving outcomes for individuals at risk for and living with cancer. A clinical trial is a type of patient-oriented clinical research study which prospectively assigns a participant, also known as a human subject, to one or more biomedical or behavioral interventions to evaluate health-related outcomes.¹ Discovering these new interventions and developing, implementing, and monitoring a clinical trial involves many groups and individuals (Box 1). Collectively their responsibility is to ensure that the rights and well-being of the research participants are protected and to advance scientific knowledge by ensuring that data generated by the trial is accurate, verifiable, and

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reproducible.^{2,3} A key role in successful implementation of a clinical trial is the study coordinator.⁴

Box 1

Key Groups and Individuals Responsible for Ensuring Good Clinical Practice (GCP)

Clinical Trial Sponsors including
Pharmaceutical Companies
Government Agencies (e.g., National Cancer Institute)
Research Teams
Principal Investigator
Sub-investigators
Research Participant
Study Coordinator (nurse or non-nurse)
Clinical Data Manager
Statistician
Research Site Collaborators
Staff/infusion nurses
Basic science and clinical laboratory staff
Radiology staff
Pharmacist(s)
Contract and billing staff
Federal Agencies
Office for Human Research Protections (OHRP)
Food and Drug Administration (FDA)

Clinical trials nursing is a specialty practice that includes a variety of roles (e.g., study coordinator, direct care nurse, nurse manager, nurse educator), settings (e.g., academic medical center, private practice, research unit), and clinical specialties (e.g., oncology, cardiology, infectious disease). The clinical trials nurse (CTN) serves as a study coordinator but may have different job titles (e.g., Research Nurse Coordinator, Clinical Research Nurse, Clinical Research Coordinator) and may be supervised by a physician, investigator, or a non-nurse research manager.⁵⁻⁹ The purpose of this article is to provide an overview of clinical trials, highlight the role of the oncology CTN (i.e., the nurse in the role of study coordinator), and share one organization's process to unite all CTNs under one nursing office.

OVERVIEW OF CLINICAL TRIALS

Good Clinical Practice (GCP) is an international ethical and scientific set of standards for the design and conduct of research involving humans including: protocol design, conduct, performance, monitoring, auditing, recording, analyses, and reporting. It includes both regulations, which are binding, and guidelines or guidances, which are not binding, though

recommended to be followed. In response to historical events of the past, regulations and guidelines have been developed (Box 2).^{2–3}

Box 2

U.S. Regulations Related to Clinical Trials

Title 45 Part 46

Subpart A: Protection of Human Subjects (1974, revised in 1981, 1991, 2005); also referred to as the Common Rule (1991)

Subpart B: Pregnant Women, Human Fetuses and Neonates in Research (1975, revised 2001)

Subpart C: Biomedical and Behavioral Research Involving Prisoners as Subjects (1978)

Subpart D: Children Involved as Subjects in Research (1983)

Subpart E: Registration of IRBs (2009)

Title 21

Part 11: Electronic Records; Electronic Signatures

Part 50: Protection of Human Subjects

Part 54: Financial Disclosure by Clinical Investigators

Part 56: Institutional Review Boards

Part 312: Investigational New Drug Application

Part 600: Biologic Products

Part 812: Investigational Drug Exemptions

Several groups with regulatory authority are involved in the conduct of clinical trials in the United States (U.S.). In the Code of Federal Regulations (CFR), the two main titles related to clinical trials are Title 45 (Public Welfare) and Title 21 (Food and Drugs). Guidance documents describe an agency's interpretation of or policy on a regulatory issue. Title 45 Part 46 is interpreted by the Office for Human Research Protections. The Food and Drug Administration (FDA) interprets Title 21 and its subparts.^{11–12}

There are five types of clinical trials (Table 1).^{13,14} Treatment clinical trials can further be characterized by phases (Table 2).^{14–16} Advancements in cancer biology, genomic profiling and the development of molecularly targeted agents (MTAs) have led trialists to re-think traditional trial designs. The emergence of basket, umbrella, and adaptive trials are examples of novel designs now being used in oncology clinical trials (Table 3).^{17–18}

PROTOCOL DEVELOPMENT AND REVIEW PROCESS

A protocol is the written detailed action plan that provides background about the clinical trial, specifies trial objectives, describes the trial's design and organization, and ensures that trial procedures are carried out consistently, protecting the research participant and providing appropriate data to answer the trial objectives. Box 3 outlines the various sections of a protocol. Protocols undergo various reviews prior to participant enrollment. Some protocols will undergo a scientific review (e.g., NCI-designated cancer centers) and some will need to have additional safety reviews:

- Radiation safety review if ionizing radiation is used at a frequency greater than standard of care
- Institutional Biosafety Committee (IBC) and Office of Biotechnology Activities (OBA) if human gene transfer is a component of the trial
- Sponsor review if the protocol was written by an investigator and not the sponsor (e.g., NCI sponsored trials).¹⁹

Box 3

Content of a Protocol – Section titles will vary based on the clinical trial sponsor or Institutional Review Board (IRB)

Title page
 Précis/Synopsis
 Table of contents including subsections and accurate pagination
 Objectives – primary and secondary
 Background Information
 Study design and methods
 Inclusion & exclusion criteria
 Clinical and laboratory methods
 Collection and storage of human specimens or data
 Statistical analysis
 Human subjects protection
 Privacy and confidentiality
 Pharmaceutical interventions
 Event reporting requirements
 Data and safety monitoring plan
 Data/record management
 Compensation
 References
 Appendices

All clinical trial protocols including the informed consent (IC) document undergo an ethical review by an Institutional Review Board (IRB) prior to their implementation. The IRB is a committee charged with the review of human subjects research. Their primary mandate is to protect and safeguard the rights and welfare of human subjects. Internationally, the IRB may be known by other names such as ethical review board or research ethics committee.^{19,20} It is important to note that a clinical trial cannot begin to enroll participants until it has been approved by the IRB.

INFORMED CONSENT

Informed consent (IC) is a legal and ethical requirement for most health care matters and when conducting clinical research. Informed consent is having the capacity to agree for one's self to participate in a given situation (e.g., clinical research). Informed consent is an

important process in the clinical research.²¹ The IC document is a written tool used by the investigator and/or other research team members to guide and reinforce the discussion with a patient about a research study. The IC document includes 8 required and 6 additional elements depending upon the type of study and IRB policy (Box 4).^{11, 22} Each IRB has an IC document template that will need to be used. When working on industry sponsored trials or a trial that is conducted at multiple sites (i.e., multi-site trial), a sample IC document is provided to each investigator for re-formatting per the reviewing IRB's template.

Box 4

Elements of an Informed Consent Document(21 CFR 50 and 45 CFR 46):

8 essential elements

A statement disclosing that the study involves research including:

- explanation of the purpose of the research
- invitation to participate
- expected duration of participation
- description of procedures to be followed
- identification of any procedures that are experimental (eg, MRI that would not be done as part of standard of care, but for research only)

Description of any foreseeable risks/discomforts

Description of any benefits to patient or others

Disclosure of any appropriate alternatives to study participation (eg, standard comfort measures)

How patient's confidentiality will be maintained

For research that involves more than minimal risk, an explanation regarding compensation if injury occurs, what that compensation is and how to obtain further information

Contact persons for questions related to research and research subject's rights

A statement regarding the voluntary nature of participation including that refusal to participate won't involve any penalty or loss of benefit to the patient

For Applicable Clinical Trials under the Food and Drug Administration Amendment Act (sections 505 or 351), the statement *A description of this clinical trial will be available on [http://\(www.clinicaltrials.gov\)](http://www.clinicaltrials.gov). This website will not include information that can identify you. At most, the website will include a summary of results. You can search this website at any time.*

6 additional elements

The intervention or procedure may cause unforeseeable risks (e.g., risk to fetus if patient should become pregnant)

Circumstance for termination of participation by the investigator (e.g., non-compliance with protocol's safety assessments, sponsor terminates an Investigational New Drug application)

Additional costs to the patient from participation

Consequences of the patient's decision to discontinue research participation

Statement that the patient will be notified of significant new findings that may impact their decision to continue participation

Approximate number of subjects

An individual's voluntary agreement to participate in a clinical trial is demonstrated by their signature on the IC document; this is referred to as obtaining consent. However informed consent is an ongoing process of communication and mutual understanding between an individual and investigator. The research participant needs to be provided with additional

pertinent new information (e.g., new risks, new procedures) throughout their participation on a clinical trial in order to make a decision to remain on the clinical trial.

The advancements in genomic profiling not only impact trial design, but the IC document and process as well. The National Human Genome Research Institute (NHGRI) recommends that the following be considered when addressing informed consent:

- Broad Versus Specific Consent
- Considerations for Families
- Considerations for Identifiable Populations
- Studies Involving Children
- Studies Involving Participants Who Cannot Give Consent
- Data and Sample Sharing Through Data Repositories and Biobanks
- Return of Results to Participants.²²

THE RESEARCH TEAM

Once the IC document is signed, protocol-specific procedures for eligibility screening will begin. If eligible, the intervention begins, data is collected, monitoring and quality control activities occur, participants are removed from the protocol based on pre-specified criteria, and data is analyzed. The results may be published and, if applicable, the results are reported in ClinicalTrials.gov, a registry for publicly and privately supported clinical studies. It is the research team that orchestrates these activities. It is essential for all individuals involved in clinical research to have knowledge and understanding of research-related laws and regulations to ensure GCP.^{24–26}

Every clinical trial has a Principal Investigator (PI) who is accountable for the overall conduct of the trial and will enroll research participants. Other team members may include: sub-investigators, study coordinator (nurse or non-nurse), clinical data manager, and statistician. The types of individuals and responsibilities vary based on the clinical setting. Table 4 outlines the general responsibilities of the PI, study coordinator, and research participant.^{24–29} It is important to note that U.S. regulations only outline the role of the Investigator, not other research team members.

ONCOLOGY CLINICAL TRIALS NURSE

In the 1960's, early chemotherapy clinical trials provided new roles for nurses. The oncology nurse needed to develop new skills and new partnerships with physician investigators while caring for patients on clinical trials. This not only included administering investigational agent(s) but also coordinating the clinical trial.³⁰ As a nurse, the oncology CTN must adhere to the American Nursing Association Scope and Standards of Practice and Code of Ethics along with their state's Practice Act. In addition to the responsibilities of the study coordinator listed in Table 4, the oncology CTN will:

- Provide and coordinate the care of the research participant

- Know the disease(s) being studied
- Understand the basics of genomics and molecularly targeted therapies including implications for participant education and informed consent
- Assess adverse events using the Common Terminology Criteria for Adverse Events (CTCAE)
- Manage toxicities within scope of license and protocol
- Educate research staff and collaborators on an ongoing basis
- Educate research participants and their significant others about:
 - Underlying disease process(es)
 - Clinical trial (e.g., objectives, schema, adverse events) and their role
 - Expectations for cure, control, palliation or no benefit
- Facilitate the ongoing informed consent process
- Advocate for the patient(i.e., research participant) and protocol²⁶

Based on the wide variation of how the oncology CTN role was implemented across various practice settings and with feedback from the Oncology Nursing Society (ONS) Clinical Trials Nurse Special Interest Group (CTN SIG), the ONS developed competencies for the oncology CTN. A complete set of the competencies can be found at: <https://www.ons.org/sites/default/files/ctncompetencies.pdf>.³¹ Initially published in January 2010, the ONS CTN competencies are undergoing a revision that will:

- Include new functional areas (e.g., data management) incorporating some previous categorizations
- Separate required knowledge from skills and behaviors
- Add recommended resources to aid in knowledge and competency achievement
- Add a more advanced level of competencies for those with more experience or who are functioning at a higher level than the novice CTN.

THE RE-ORGANIZATION OF CTNs: ONE INSTITUTION'S EXPERIENCE

Necessity is the mother of taking chances.

- A quote from *Roughing It* by Mark Twain, American
Author and Humorist

The Center for Cancer Research (CCR) is the basic and clinical intramural research program of the National Cancer Institute (NCI). Within the CCR is the Office of the Clinical Director (OCD) which supports CCR's clinical research program by providing biostatistical expertise, education and training, data management, auditing and monitoring activities, regulatory support and expertise, and informatics for data collection and storage.

The growth of CCR clinical research programs requiring support of the CTN has increased over the years. Historically the management of CTNs fell within the specific programs including CTN recruitment, supervision, training, personnel actions, and performance evaluations. The programs were silos in which the team functioned. By 2011, there were 74 CTNs across 13 programs, supporting 68 Principal Investigators (PIs). As the workload of one program grew there was little to no flexibility to have CTNs cross-cover from another program. The scope and volume of work was discrepant across programs. When programs expanded their research portfolio necessitating more CTN staff, the request was forwarded to the OCD for evaluation and approval. There were no standard performance evaluation metrics. Work practices for leave and attendance and telecommuting were different across programs. Communication practices were not efficient or timely. There were a multitude of reasons that supported the CCR leadership to consider centralizing the CTNs.

In 2011 the CCR leadership recognized that the organization would benefit from an integrated infrastructure for CTNs. The primary purpose was to allow nurses to report to nurses in the hopes of:

- Establishing a career path for CTNs
- Establishing core CTN competencies
- Increasing training
- Developing standard policies for time and attendance
- Allowing for the cross training required to respond to variances in workload
- Establishing an esprit de corps
- Efficiently recruiting and hiring CTNs
- Implementing human resource actions consistently
- Establishing efficient mechanisms for communication
- Ensuring collaboration with the Principal Investigators

OFFICE OF RESEARCH NURSING (ORN)

The new office would be called the Office of Research Nursing (ORN) and would become part of the Office of the Clinical Director. The Deputy Director for the CCR was sensitive to the fact that this was a major cultural shift for CTNs and the PIs. A number of town hall meetings for CTNs and PIs were held in Fall 2012 to present the idea for a new model and to elicit feedback from these stakeholders.

Building the infrastructure for this office took place between September 2012 and March 2013. The ORN was given a budget to include salaries, travel, training and supplies. A Chief needed to be recruited for the office and three team leaders needed to be hired into the ORN. The Chief was an experienced leader in nursing within the CCR with background as a CTN and nurse practitioner. The team leaders selected had a strong background in research nursing, leadership and a strong institutional knowledge. A leadership team formed and an administrative assistant hired with responsibilities for travel, supplies, management of

timecards, and facilitation of the recruitment and hiring processes. Performance evaluations were created using the ONS Competencies. The ORN Chief believed that the consolidation of nursing under nursing leadership would have the potential to develop quality CTNs to support clinical research within the organization.

LEADING CHANGE THROUGH ENGAGEMENT

In order for the new model to be successful, the Chief needed to lead change by engaging clinical research staff in a mutually supported vision of the future while being sensitive to the cultural change experienced by the CTNs and the PIs. In *Getting Change Right*, Seth Kahan shares tips for successful change:

So what's a change leader to do? Create ways for people to get together and converse. Get them participating, engaged, and involved. This is the road to personal investment, enthusiastic support, and genuine buy-in. This is how you move people across the line from "I *have* to do this" to "I *want* to do this." And that makes all the difference in the world.³²(p17)

The challenge with the reorganization was getting engagement across the research team.

On the first day in office, the Chief made appointments with each one of the 74 CTNs and interviewed them to understand their background (Box 5), motivations, and career aspirations. CTNs were asked:

- How long they had been in their jobs?
- What kept them in their jobs?
- What obstacles did they face preventing them from getting their job done?
- What was on their wish list?

Box 5

Research Nurses Demographics

Educational Background

Master's Degree in Nursing: 14

Master's Degree in Other (in addition to their nursing degree): 7

Bachelor of Science in Nursing: 52

Associate Degree: 8

Years in Nursing

< 5: 3

5–10: 12

11–15: 8

>15: 51

Certification in Nursing

Oncology Certified Nurse (OCN): 20

Bone Marrow Transplant Certified Nurse (BMTCN): 2

<p>Advanced Practice Nurse in Genetics (APNG): 2</p> <p>Certification in Clinical Research</p> <p>Certified Clinical Research Coordinator (CCRC): 1</p> <p>Certified Clinical Research Professional (CCRP): 2</p>
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Overwhelmingly, the CTNs said that what kept them in their jobs were the relationships with their colleagues including investigators and other physicians. They felt intellectually challenged by the research protocols and science, autonomous in their positions, and driven to help patients. The overriding impediment related to performing their jobs better was a lack of communication about policies and procedures. They wanted to know best practices and what other nurses were doing that improved their efficiency. Much of the information gained from these interviews was congruent with the reasons for the reorganization of the CTNs. The Chief felt comfortable knowing that the needs of the CCR and the CTNs were in alignment.

Establishing Structure

The ORN leadership team met, developed the ORN draft mission and vision statement that was presented to the CTNs for their input and feedback. This was a key first step to engaging staff in decision making for what was to be a long-term meaningful partnership between leadership and staff.

To provide a unique, cohesive team of superior research nurse specialists to carry out the mission of the CCR through a culture that supports continuing education, mentorship, professional development, and collaboration while balancing comprehensive patient coordination and quality clinical and translational research.

- Vision statement for the Office of Research Nursing,
2013

The leadership team participated in a 12 week supervisory course on self-development, program development and leading through change. Training included the legalities of supervision, conflict resolution, leadership development, forming and leading teams, and handling human resource issues. In addition, the Chief and team leads were afforded the opportunity to have three months of individual executive coaching which has proven to be invaluable for the development of the ORN.

The ORN established four teams each with a team lead (Fig 1). The ORN leadership took the following into account:

- CTN experience
- Existing research team dynamics
- Research team workload (e.g., types of protocols, phases of clinical trials, number of protocols)
- Support staff (e.g., data manager, scheduling support staff, mid-level providers)

The aim was to provide manageable teams for each team leader to supervise while supporting the vision statement of the ORN.

Communication and Transparency

An immediate response to the needs of both the CCR and the CTN was to initiate a communication plan. The ORN developed a monthly newsletter that includes staff recognition, educational opportunities, new policies/procedures, staff departures, staff hires, and regulatory updates. The newsletter is distributed via email and posted on a dedicated website. Informal staff meetings called “Coffee and Chats” began and are held monthly on three different days of the week so that all staff have an opportunity to attend. The purpose of these meetings is for staff to network, share best practices and receive up-to-date information from the leadership team. The CTNs are invited to join the meetings but not required to attend the meetings. Part of the communication plan includes the development of the ORN Wiki page. The site is maintained by the ORN Chief and contains: newsletters, listing of the nurses, their contact information, and procedures for promotion. An email distribution list with all research nurses, ORN leadership, and additional staff from the Office of the Clinical Director (e.g., Deputy Clinical Director, Nurse Educator, Protocol Support Office Director, and Quality Management Coordinator) allows rapid, thorough communication to all CTNs.

Each team leader developed relationships with their CTNs, the teams in which the team leaders worked, and the respective PIs. It was imperative to know what each individual on the research team valued and find ways to help them achieve that as quickly as possible. The team leaders attended research team and data management meetings as well as clinic when needed. The team leaders continue to meet regularly with PIs.

Quickly workgroups began to emerge comprised of staff who identified a need or a problem and developed a team to address solutions. One workgroup emerged to address documentation needs in the electronic medical record. Others workgroups developed including:

- Wellness Committee with a goal of helping CTNs strike work-life balance
- Journal Club to provide CTNs with a forum to discuss peer-reviewed literature related to oncology, nursing or clinical trials
- Model for cross-coverage and what it meant to cover for a CTN who was out of the office.

Making Changes

From its inception the ORN leadership made a strategic decision that changes in practice would be small with a likelihood of being successful and that we would build from there. It was about building trust and respecting staff input. A decision was made that all changes would be presented to the staff with rationale for the change; they would have input; and leadership would listen. The principal investigators and other stakeholders were included in the communications. We would use ‘champions’ to advocate for new ideas and change that needed to be addressed. We would communicate to the staff the final proposal and then roll

out the changes and fully communicate to all involved. The first change that was presented was standard operating procedures (SOP) for time, attendance, and telework. This process was successful, as the staff trusted the process allowing for subsequent changes. We established ground rules for conducting business including work schedule options, performance evaluations, and promotion procedures. All changes were approached in the same manner of our change management philosophy.

NOW THAT WE HAVE ENGAGEMENT, TIME TO GET DOWN TO BUSINESS

A priority of the CCR was to improve cross coverage and flexibility to cover workload. There were 4 programs that included only one CTN. We paired these single CTN teams with other CTN(s) to cover workload in times of absences. We also identified the need to have a senior resource CTN who could be deployed to teams for various reasons (e.g., cover for CTN out on extended leave, audit assistance, or coverage due to a temporary increase in workload). This resource CTN was available to precept new staff. Additionally, all team leaders ensured that they had a working knowledge of their team's protocols so that they could backup a CTN if necessary.

There had been a promotion process in place at the CCR for CTNs who want to be considered for promotion. The process was evaluated by leadership and senior staff who had previously gone through the process. Feedback was elicited from staff and the process was finalized. There are 5 nurses promoted using the new promotion process incorporating a leadership initiative as part of their senior CTN status.

New CTN orientation has been redesigned. Each new CTN is assigned a preceptor. New CTN orientation procedures and standardized checklists have been developed to guide the new CTN and their preceptor. An integral piece of the orientation is the formalized clinical trial training provided by the Nurse Educator.

COMPETENCY ASSESSMENT AND VALIDATION

Once the basic infrastructure of the ORN was created and engagement started, the next initiative was competency assessment and validation. Working with the CCR Nurse Educator, the ORN embarked on developing behavioral indicators for 2 of the 9 ONS competencies (i.e., professional development and documentation) using working groups that included CTNs and leadership. A validation tool was created (Table 5) and the Nurse Educator developed a facilitator's guide (Table 6) with input from ORN leadership.

The Nurse Educator validated the competency for the ORN Chief and each of the team leaders using the facilitator's guide. Time was spent discussing how the team leaders would use the guide to validate the research nurses competency. In January 2015 CTNs were notified that competency sign off was to be performed in March. Between January and March 2015 educational sessions were offered to staff and by the end of March all CTNs were signed off on their professional development competency by their team leader. Additional competency validation is ongoing.

ASSESSMENT OF THE ORN AND FUTURE PLANS

Three years following the inception of the ORN, consolidating the CTNs under one office has been viewed as success by the CTNs and the research teams. This new infrastructure was supported by an organizational commitment to optimize this key resource for the clinical program. Future strategic direction includes completion of competency assessment and validation using the ONS Competencies, development of a workload assessment tool, development of a training and resource manual, and continued commitment to improve communication.

SUMMARY

Clinical research is the foundation for improving human health. Clinical trials, a type of clinical research, explore ways to prevent, screen, diagnose, treat and improve quality of life for individuals with a chronic illness. Protecting research participants and ensuring quality data are the responsibility of many individuals and groups. Participant protection includes the ethical review of a protocol and the informed consent of the participant. The protocol serves as a written detailed action plan that supports the scientific rationale for conducting the trial and outlines all trial procedures to be conducted all to ensure the participant's safety and the quality of the data. A key member of the oncology research team is the oncology CTN who may or may not be supervised by a nurse. Using the process of engagement, one organization has been able to restructure the CTNs into a nurse-supervisor model with direct benefits to the CTN.

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KEY POINTS

- Genomic profiling and the development of molecularly targeted agents (MTAs) have led to novel designs for oncology clinical trials.
- Ensuring human subject protections and quality data are responsibilities for all individuals involved in clinical trials, however the Principal Investigator (PI) is ultimately accountable for the overall conduct of the trial.
- Oncology Clinical Trials Nurses (CTNs) are critical to the implementation of oncology clinical trials.
- Competencies developed by the Oncology Nursing Society help define the specialized role of the oncology Clinical Trials Nurse (CTN).

Fig. 1.
Organizational Chart for the Office of Research Nursing

Table 1

Types of Clinical Trials

Trial Type	Purpose(s)	Example(s)
Prevention	Evaluate better ways to prevent a disease [*] from developing or returning	Vaccine (e.g., HPV vaccine) Exercise
Screening	Discover the best ways to detect a disease [*] in the general population, or for individuals who have a higher than normal risk of developing a disease, before symptoms start	Laboratory test (e.g., BRCA1) Imaging (e.g., mammogram) Health history (e.g., pedigree)
Diagnostic	Evaluate better ways to identify a particular disease [*]	Genetic tests (e.g., VHL syndrome) Imaging tests (e.g., PET scan)
Quality of Life/ Supportive Care	Explore ways to improve the comfort and the quality of life for individuals with a chronic illness	Anti-emetic Support group
Treatment	Develop better interventions for disease [*]	Drug Vaccine Device Surgery Radiation Psychotherapy Combination modalities

^{*} Disease includes a disorder or health condition

Abbreviations: HPV, human papillomavirus; VHL, Von Hippel Lindau (VHL), BRCA1, BReast CAncer *genes* 1; PET, Positron emission tomography

Table 2

Phases of Clinical Trials

Phase	Goals	Traditional Design
I	Determine dosing in humans - known as the maximum tolerated dose (MTD); conducted in adults before children Assess safety Evaluate pharmacokinetics (PKs) and pharmacodynamics (PDs) May also be used to evaluate new treatment schedule, new drug combination strategy, and new multimodality regimen	Open label, non-randomized, dose escalation with cohorts of 3–6 research participants - known as a 3 + 3 design Increase dose gradually, most commonly using a modified Fibonacci schema Low starting dose based on the animal models as not likely to cause serious toxicity
II	Provide initial assessment of efficacy or clinical activity Further define safety and toxicity	Open label, one dose level based on the MTD - also known as the recommended phase 2 dose (RP2D) Most commonly a 2 stage design with an early stopping rule Increasing use of randomized designs
III	Efficacy compared to standard therapy Further evaluation of safety	Randomization with or without blinding May include stratification based on disease specific prognostic factors (eg, hormone receptor status in breast cancer) or other factors (eg, age, gender)

Table 3

Trials Designs for Targeted Therapies

Trial Type	Description	Example
Basket Trial	Test a MTA on the same genomic mutation regardless of tumor histology	NCI-MATCH (ClinicalTrials.gov Identifier: NCT02465060)
Umbrella Trial	Test a MTA on a single tumor type/histology with different genomic mutations	Lung-MAP (ClinicalTrials.gov Identifier: NCT02154490)
Adaptive designs	Use accumulating data to decide how to modify aspects of the trial on an ongoing basis without undermining the validity and integrity of the trial	I-SPY 2 (ClinicalTrials.gov Identifier: NCT01042379)

MTA, Molecular Target Agent; NCI, National Cancer Institute; MATCH, Molecular Analysis for Therapy Choice; Lung-Map, Lung Cancer Master Protocol; I-SPY 2 Trial, Investigation of Serial Studies to Predict Your Therapeutic Response With Imaging And moLecular Analysis 2

Table 4**Responsibilities of the Principal Investigator, Study Coordinator, and Research Participant**

Role	General Responsibilities
Principal Investigator (PI)	Comply with all applicable federal regulations and state laws impacting the protection of human subjects Comply with all applicable IRB policies, procedures, decisions, conditions, and requirements Conduct study in accordance with the current IRB-approved protocol Design the clinical trial and/or provide study oversight Personally conduct and supervise the clinical trial
Study Coordinator	Recruit and retain research participant Schedule protocol-specific procedures Secure and reinforce informed consent Prepare for and participate in monitoring visits and audits Ensure integrity of protocol is maintained by enforcing timelines for study visits and other procedures Maintain regulatory files Assist PI in submitting protocol & consent for initial review, continuing review & amendments Report serious adverse events and unanticipated problems Participate in data management & data quality assurance (QA)
Research Participant	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 Know when the study begins and ends Follow directions for all protocol related procedures Show up at scheduled appointments on time or inform research staff within a reasonable time if they need to reschedule Report symptoms and other problems they experience during the study Provide truthful answers to questions asked throughout the study Inform staff if they decide to withdraw from the study

Table 5

Professional Development Competency Validation Sign-off Log

Rating Indicators: 1 = Requires assistance and supervision; 2 = Requires supervision; 3 = Independent; 4 = Assists and instructs others <i>Note: See Facilitator's guide for specific criteria for each indicator and rating.</i>				
Assessment method used for validation: D = Demonstration; DR = Document Review, V = Verbalization; O = Other (specify)				
Behavioral Indicators	Assessment Method	Rating		Comments
		Self	Validator	
1. Participate in at least 4 hours annually of research educational activities and document in the Professional Development log.	DR			
2. Participate in at least 4 hours annually of oncology nursing educational activities and document in the Professional Development log.	DR			
3. Maintain curriculum vitae (CV).	DR			
4. Identify professional organizations related to clinical trials and oncology nursing.	V			
5. Use resources related to clinical trials, oncology and nursing practice on an ongoing basis.	V			

Table 6

Sample of Professional Development Competency Facilitator's Guide

Indicator #2: Participate in at least 4 hours annually of oncology nursing educational activities Oncology nursing or professional development activities include any of the following: <ul style="list-style-type: none"> ONS Congress, Chapter meetings, and clinical webinars Other disease specialty conferences/meetings Nursing Grand Rounds (offered 3–4 times per year) Brown Bag Lunch (offered monthly September – June) CC genetics & genomics courses (basic or intermediate) Professional Development Series (offered 3–4 times per year) Other CE activities (i.e., reading a journal article that offers CE units) Oncology nursing or professional development activities <i>do not</i> include: <ul style="list-style-type: none"> CPR/ACLS/PALS 		
Instructions: Using the Research Nurse's professional development (PD) log for the previous 12 months, evaluate the indicator using the criteria below.		
1	Requires assistance and supervision	0–3.5 hours listed in the last quarter
2	Requires supervision	0.5–3.5 hours listed to reflect ongoing learning (i.e., not just in the last quarter)
3	Independent	4 or more hours listed to reflect ongoing learning (i.e., not just in the last quarter)
4	Assists and instructs others	N/A