

# Adding Pharmaceutical Clinical Research Studies to Oncology Practice

By Ruth Ann Nysten, PhD

## Abstract

This article describes the considerations for making the decision to implement clinical research trials into an oncology practice.

Written for the aspiring physician-investigator, it is an informative and resourceful piece for those wanting to know more about this process.

## Benefits of Participating in Clinical Research Trials

The conduct of clinical trials is a US federal mandate that precedes approval of all prescription drugs by the Food and Drug Administration (FDA). Participation in clinical trials offers several advantages for the practicing oncologist. Conducting clinical research trials provides both physicians and patients with treatment options not available with approved products. Gaining experience in the pre-approval stage with novel therapies or combination regimens may provide insights into new clinical therapeutics. For patients with conditions that are refractory to currently available treatments, participating in clinical research may provide the patient an option that may save his or her life.

Since 1990, the amount invested in research and development of new drugs in by US Pharmaceutical Manufacturers has more than tripled and reached more than 30 billion dollars worldwide. Of this 30 billion, more than 23 billion is spent on US based research, with a substantial majority spent on human clinical trials.<sup>1</sup>

## The Role of the Physician in the Clinical Drug Development Process

Physicians with active medical practices are needed to conduct clinical trials sponsored by private pharmaceutical companies, as well as federally-funded programs, supported by federal agencies such as the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), and the Veterans's Administration. The greatest need for physicians in clinical research trials is in the conduct of Phase III safety and efficacy trials that typically compare innovative treatments (investigational) with either approved products, or placebo. Physicians in a single-site medical practice may have opportunity equal to that of a large, multi-site practice, or academic medical center, to contribute not only patients but also to the science. Community oncology practices represent the usual

care setting, thus it is important that phase III trials include participation of patients and practitioners from this setting before new treatments can be approved for general/commercial use.

## Achieving Optimal Success

Achieving optimal success requires investment in time, personnel and process. Successful investigators will establish an effective infrastructure, and educate themselves and their clinical trial staff.

## Step 1: Establishing an Effective Infrastructure

Establishing an effective infrastructure is essential to the success of a trial. The infrastructure must include knowledgeable, and adequately trained personnel to fulfill the roles required in the study, and a well-organized,

**Table 1: Clinical Study Site Personnel**

Personnel	Typical Roles and Responsibilities
Investigator	<ul style="list-style-type: none"> <li>• Has overall responsibility, accountability and liability for all aspects of a clinical trial</li> <li>• Most often practices medicine as a licensed physician</li> </ul>
Clinical Research Coordinator	<ul style="list-style-type: none"> <li>• Accept responsibility for and perform clinical study functions, as delegated by an investigator</li> </ul>
Sub-investigators	<ul style="list-style-type: none"> <li>• Accept responsibility for and perform clinical study functions, as delegated by an investigator</li> </ul>
Administrator	<ul style="list-style-type: none"> <li>• Scheduling</li> <li>• Documentation support</li> </ul>
Pharmacist (optional)	<ul style="list-style-type: none"> <li>• Stores, handles and generates the required documentation for investigational drug supplies</li> </ul>

defined, and documented process for conducting trials.

### **Personnel**

Appropriate personnel for a clinical trial have the most direct impact on its success.

Table 1 summarizes typical study site personnel and delegated responsibilities.

### **The Clinical Research Coordinator**

The most valuable player (MVP) award at clinical research centers most often is given to the clinical research coordinator (CRC). It is critical for physician-investigators to hire a CRC. Several associations, including the Association of Clinical Research Professionals (ACRP, <[www.acrpn.org](http://www.acrpn.org)>), and the Society of Clinical Research Associates (SOCRA <[www.socra.org](http://www.socra.org)>) provide useful information about CRCs. Each association includes CRCs as members, and each sponsors training and certification programs for CRCs. An experienced CRC's salary will typically range from \$40,000-80,000, depending on geographic location, education and experience. For details on salary data see <http://www.acrpn.org/publications/salary.htm>. An experienced CRC is an invaluable asset in establishing a clinical trial component into an active practice, and will generate far more revenue than his/her salary, once the trial process is established. Expect to make an investment in a CRC.

### **Sub-investigator**

Sub-investigators are often licensed physicians or other licensed health-care providers who can perform medical procedures or other study requirements on behalf of the investigator. The principal investigator is responsible for providing training to sub-investigators. Sub-investigators are an option available to the principal investigator to support the conduct of a trial, but are not as critical as the CRC.

### **Research Pharmacist**

Many institutions, including universities, academic medical centers and large clinics have pharmacists who have been, or can be trained in the duties of a clinical research pharmacist. Research pharmacist activities are described in the International Committee on Harmonization (ICH) Good Clinical Practice (GCP) Guideline, sections 4.6, Investigational Product(s), 5.12 Information on Investigational Product(s), 5.13 Manufacturing, Packaging, Labeling, and Coding Investigational Product(s), and 5.14, Supplying and Handling Investigational Products ([www.ich.org](http://www.ich.org)). If a pharmacist is not available, the investigator (or designate) assumes the responsibilities that may otherwise be delegated to a pharmacist.

Word of caution about study personnel: While the investigator may delegate any of his/her study responsibilities to a research coordinator, sub-investigator, or pharmacist the responsibilities are not abdicated.

### **Clinical Trial Business Process**

Interfacing clinical trials into a functioning medical practice will require some adjustment and changes in several key areas including patient scheduling, and office staff knowledge. Equally important is the establishment of standard operating procedures.

### **Patient scheduling**

Patient visits in clinical trial protocols must be scheduled as defined in the study protocol. Any deviation from the protocol requirements can, and often does result in losing the patient and invalidation of some or all of the patient's data. Therefore, it is critical to give priority to scheduling and ensuring clinical trial patients complete the required visits.

### **Office staff knowledge**

While it is typical in a group or large office setting to have selected individuals managing the clinical

trial, it is essential that all office staff members are adequately informed and knowledgeable about the trial, to avoid inadvertent loss of patients and or study data.

Any person who may potentially have contact with a patient in a clinical study must be aware that study patient scheduling, the need to speak with the clinical research coordinator or physician investigator, must receive immediate priority treatment. This is particularly the case if the study subject (participant) contacts the office to report adverse events. Because the safety of a study subject is of utmost importance, clear communication processes must be established to ensure effective protection of study participants.

### **Establishment of Written Standard Operating Procedures**

It is highly recommended that investigators establish written standard operating procedures (SOPs) for conducting clinical trials. Establishing SOPs will:

- Establish a standard of excellence for all trials.
- Ensure that processes are done consistently and accurately.
- Facilitate compliance with federal regulations and guidelines.
- Demonstrate the investigators commitment to trials.
- Support the training of all study personnel.

Several industry resources are available to assist physician-investigators with the development of SOPs, including Research Dynamics Consulting Group Ltd ([www.resdyn.com](http://www.resdyn.com)), which offers electronic templates that can be used to easily customize SOPs.

### **Step 2: Getting Trained and Becoming Knowledgeable**

To be successful in clinical research, physicians must be trained in the current requirements

of clinical trial methodology and process. This training is available from a variety of sources including industry associations such as The Drug Information Association (DIA, www.diahome.org), the American Academy of Pharmaceutical Physicians (AAPP, www.aapp.org), ACRP and SOCRA, mentioned previously, as well as other commercial and private training organizations. An Internet search on "clinical research education" can provide multiple training resource options.

**Fact:** Being assigned to serve as a sub-investigator and perform a few study procedures to gain "clinical research experience" during a medical school residency is not remotely close to the responsibilities of being principal investigator. The risk of being untrained in clinical research is too great to assume in the current environment of increased regulatory scrutiny.

**Good Clinical Practice Defined**

All clinical trials, regardless of the source of funding or sponsor, must be conducted in compliance with Good Clinical Practices. It is critical that physicians understand that the term Good Clinical Practice, or "GCP" is different in clinical trials than it is generally understood in the practice of medicine (www.ich.org). In the practice of medicine, good clinical practice is generally understood to encompass professional behaviors including employing the accepted standard of care to patients.

In contrast, conducting clinical trials in compliance with Good Clinical Practices, includes those behaviors accepted in medical practice, but additionally requires sound knowledge of and compliance with specific FDA and international regulations and guidelines. The essential requirements that physician investigators must be knowledgeable of to ensure GCP compliance include those listed in Table 2.

Compliance with the federal regulations must be taken seriously. Non-compliance or violation of these federal statutes may result in disqualification by the FDA, as well as civil or criminal prosecution.

**Learn the Requirements of the Sponsoring Organization**

Because pharmaceutical sponsors are required by the FDA and international regulations and guidelines to evaluate and select physician investigators to conduct clinical trials, it is imperative that prospective physician-investigator are knowledgeable about the assessment criteria. Typical areas/items assessed include:

- Investigator and staff qualifications.
- Availability of protocol-eligible subjects.
- Equipment and facilities.
- Knowledge of GCP requirements.
- Familiarity with clinical research requirements, including previous experience with an IRB.
- Willingness to provide financial disclosure.
- Interest, motivation and cooperation.

**An Opportunity Coupled With Challenge**

The decision to participate in clinical trials should include an

**Table 2: Federal Regulations Essential to Clinical Trials**

<b>Regulation or Guideline</b>	<b>Summary of Essential Content</b>
21 CFR 11 Electronic records; electronic signatures	• Controls and requirements for electronic data.
21 CFR 50 Protection of Human Subjects	• Informed consent requirements.
21 CFR 54 Financial Disclosure by Clinical Investigators	• Requirements for investigators to disclose financial relationships with sponsors.
21 CFR 56 Institutional Review Boards	• Requirements for independent review of human research.
45 CFR 46 Protection of Human Subjects	• Note: Applies only to investigators conducting federally-funded research. Includes both human subject protection requirements as well as institutional review board requirements.
21 CFR 312 Investigational New Drugs	• Defines the scope of human research under jurisdiction by the FDA; outlines the responsibilities of investigators and sponsors in clinical trials.
The ICH (International Conference on Harmonization) GCP Guideline	• Outlines all Good Clinical Practice requirements for IRBs, investigators, sponsors, including protocol requirements, and documentation requirements for clinical trials.
The FDA Information Sheets for Clinical Investigators and Institutional Review Boards	• Provides a detailed explanation of the FDA's interpretation of the requirements in clinical trials.

**Note:** "CFR" refers to the United States Code of Federal Regulations

assessment of the challenges and opportunities, as well as costs/return on investment.

As with any new business, challenges abound in clinical research, and will include:

1. The need for trained personnel.
2. Modifications and enhancements to the established medical practice process to accommodate and ensure success with the clinical trial.
3. An investment of time and money.

The opportunities can be worth the challenge. Participation in clinical trials may offer the practicing oncologist these opportunities:

1. Expansion of professional knowledge in research and therapeutics.
2. Direct contribution to the body of scientific knowledge.
3. Improved patient outcomes.
4. Enhanced revenues.

#### **Conclusion**

Clinical research differs significantly from daily medical practice and requires an investment in personnel, process, training and time. If physician investigators are committed to involvement in clinical trials and are willing to make the required investments, participation can bring professional, financial and patient care enhancements to an active medical practice.

#### **References**

1. Pharmaceutical Research and Manufacturers of America, 2002 *Industry Profile*, PhRMA, Washington, DC, 2002.

#### **Author bio**

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