

# ACCP

## The Clinical Pharmacist as Principal Investigator: A Commentary from the American College of Clinical Pharmacy

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### Introduction

Research is critical to advancing the practice of pharmacy. Indeed, the last three decades contain many examples where seminal research papers authored by clinical pharmacists have advanced pharmacy care and improved patient outcomes. Whereas many clinical pharmacists have established strong research programs, there must be continued efforts to increase the number of highly competent pharmacist researchers by reducing barriers into a research career and improving the quality of research training programs. The American College of Clinical Pharmacy (ACCP) continues to receive inquiries regarding the requisites for a pharmacist to serve as the principal investigator (PI) for industry-sponsored research. This paper summarizes Food and Drug Administration (FDA) policies regarding the pharmacist's ability to serve as PI on clinical drug research; presents a brief view on this issue from the perspective of the pharmaceutical industry; describes FDA regulations governing clinical research, and the PI's responsibilities in meeting those regulations; and provides advice to clinical pharmacists who desire to serve as PIs on clinical drug research sponsored by the pharmaceutical industry.

### History of the Clinical Pharmacist as Principal Investigator

#### The ACCP's role as an advocate for the clinical

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pharmacist as PI began in 1983. At that time, there was generally a great deal of reluctance within the pharmaceutical industry to allow pharmacists to function as PIs. Some clinical pharmacists were successfully participating as PIs in industry-sponsored and FDA-regulated clinical research, whereas others were being told by some industry sponsors that they interpreted FDA regulations to allow only physicians to be PIs. To clarify this matter, then-ACCP president Peter H. Vlasses, Pharm. D., wrote then-FDA Commissioner Arthur Hull Hayes, M.D., regarding FDA regulations on the issue. Stuart L. Nightingale, M.D., then-FDA Associate Commissioner for Health Affairs, responded by writing, "It has long been FDA policy to accept Doctors of Pharmacy as primary investigators of studies of investigational drugs within their areas of expertise." The FDA response noted that a person "licensed to diagnose and treat disease be officially associated with the study" as a coinvestigator (Figure 1).<sup>1</sup> Subsequently, many clinical pharmacists used the correspondence to educate industry research sponsors and gain the ability to serve as PIs.

Some companies continued to have internal policies that required a physician to be the PI. Others interpreted the FDA letter to apply only to pharmacokinetic studies and not to clinical trials. To clarify the latter point, Dr. Vlasses again corresponded with the FDA. Dr. Nightingale responded, stating, "Doctors of Pharmacy may serve as clinical investigators for both clinical pharmacology studies and clinical trials of a drug provided they do so in conjunction with a person licensed to diagnose and treat disease," again emphasizing that a physician must be a subinvestigator to assess the patient and make medical decisions.<sup>2</sup> In 1990, correspondence from the FDA to the American Association of Colleges of Pharmacy reiterated that "pharmacists can serve as principal investigators in any clinical trial" (Figure 2).



DEPARTMENT OF HEALTH &amp; HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

MAY 10 1983

Peter H. Vlases, Pharm.D.  
Associate Director, Clinical Pharmacology Unit  
Thomas Jefferson University Hospital  
11th and Walnut Streets  
Philadelphia, PA 19107

Dear Dr. Vlases:

Your letter of February 24, 1983 to Dr. Hayes has been referred to me for response. In that letter you posed the question whether Doctors of Pharmacy (Pharm.D.s) may serve as investigators in clinical pharmacological studies of investigational drugs. You noted that you have received varying interpretations of our regulations on this point from different manufacturers who sponsor clinical pharmacological studies.

It has long been FDA policy to accept Doctors of Pharmacy as primary investigators of studies of investigational drugs within their areas of expertise. Because such studies may require the diagnosis of disease and the recognition and treatment of adverse reactions or other medical incidents occurring during the course of the study, we have required that a person licensed to diagnose and treat disease be officially associated with the study to be performed. This is ordinarily done by naming such an individual in item 6(f) of the Form FD-1572 as being responsible to the principal investigator of record. Alternatively, both the Doctor of Pharmacy and the licensed individual may sign the Form FD-1572 as co-investigators, having equal responsibility in the performance of the study in question.

I trust that this clarifies FDA policy on the matter.

Sincerely yours,

Stuart L. Nightingale, M.D.  
Associate Commissioner for  
Health Affairs

Figure 1. 1983 response letter from the FDA addressing participation of clinical pharmacists as PIs.

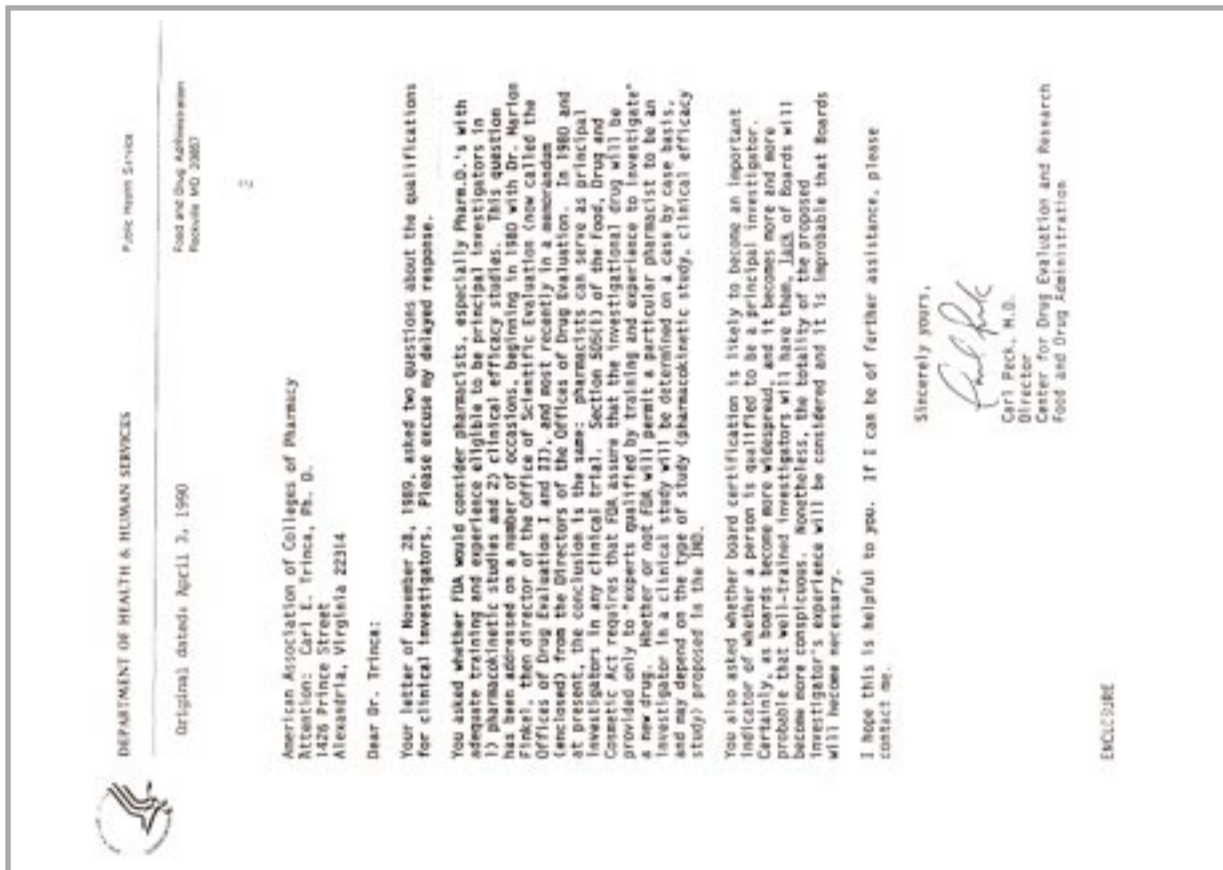


Figure 2. 1989 and 1990 response letters from the FDA reiterating that clinical pharmacists can serve as PIs in clinical trials.

Fifteen years later, many clinical pharmacists have served and continue to serve as PIs in human trials. Nonetheless, it is important to emphasize that one's academic degree alone—whether M.D. or Pharm.D.—does not qualify the individual to serve as PI. The person's overall training and experience, complemented by their research environment, are integral to their designation as PI. As noted by Dr. Nightingale, the FDA may “reject any investigator as unsuitable as part of [the] review process” if their overall portfolio is insufficient to demonstrate that they possess the knowledge, skills, and experience needed to assume the significant responsibilities of PI.<sup>2</sup>

### Current Industry Perspective

To better understand current industry policies regarding pharmacists as PIs, a short, informal survey was administered by telephone to a small number of pharmaceutical companies. Information was obtained from five companies and suggests that most companies do not have specific policies that exclude pharmacists from functioning as PIs. However, the general consensus was that pharmacists were used primarily for pharmacokinetic studies and not for other types of clinical trials. In most instances, the program manager or study team leader makes the decision regarding which investigators to approach as PIs based on their overall qualifications. If a pharmacist can demonstrate his/her expertise in a therapeutic area (as outlined later), and his/her ability to enroll the required number of qualified subjects into the clinical trial within an established time period, it would appear that most pharmaceutical companies will allow a pharmacist to serve as the PI for a study.

If the contact at a particular company states that a pharmacist may not serve as a PI, it may be worth inquiring about this policy. It could be that the decision maker is unaware of FDA's policy regarding pharmacists as PIs. Such information could influence the decision of the study manager, especially if there is no company policy that precludes pharmacists from functioning as PIs.

Given the importance of investigator experience and qualifications to their designation as PI, the remainder of this paper centers on the capabilities and responsibilities (including FDA regulations) needed to serve in this capacity.

### FDA Policies, Regulations, and Guidelines for Investigators

### FDA's Role and Responsibilities

Investigations of new chemical entities and dosage forms in the United States are regulated by the FDA. A qualified PI must have a comprehensive understanding of FDA policies and regulations regarding the conduct of clinical trials and the use of an investigational new drug. The PI must also demonstrate his/her ability to consistently abide by these policies and regulations. The Center for Drug Evaluation and Research (CDER) monitors the clinical development of drugs, whereas the Center for Biologics Evaluation and Research (CBER) supervises the clinical development of biologics, including most biotechnology products. Regulations are designed so clinical trials can proceed with new compounds, but with adequate safeguards to protect the health and safety of study subjects in particular and the well-being of the American people in general. Society benefits from the availability of new medicines in a timely, cost-efficient manner, but there must be protection from unanticipated adverse reactions or impure compounds. Information about CDER and CBER can be obtained from their respective Web sites: [www.fda.gov/cder](http://www.fda.gov/cder) and [www.fda.gov/cber](http://www.fda.gov/cber). An excellent review of the new drug development process is found in the *CDER Handbook*, available from CDER's Web site.

The document, “Guidance for Industry: E6—Good Clinical Practice: Consolidated Guidance,” was developed by the Expert Working Group (Efficacy) of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The guidance encompasses the ethical tenets of the Declaration of Helsinki, as well as good clinical practices within the European Union, Japan, Australia, Canada, the Nordic countries, and the World Health Organization. It also represents the FDA's current thinking on good clinical practices. This Good Clinical Practice (GCP) guidance establishes standards for all aspects of the conduct of clinical studies; seeks to provide assurance that the data and results of these studies are credible and accurate; and assures that the rights, integrity, and confidentiality of trial subjects are protected.

Investigators are defined in the GCP guidance as the persons responsible for the conduct of a clinical trial at a given site. If that trial is conducted by a team of individuals, the PI is the responsible team leader. Subinvestigators are individual team members designated and

supervised by the PI to perform critical trial-related procedures and/or make important study-related decisions. In the same document, a clinical trial or study is defined as any investigation in human subjects intended to discover or verify the clinical, pharmacological, and/or pharmacodynamic effects of an investigational product.

#### FDA Regulations and Policies for Investigators

The FDA's overwhelming principle of clinical investigation is that the rights, safety, and well-being of trial subjects should prevail over the interests of science and society. The medical care given to, and medical decisions made on behalf of, study subjects must always be the responsibility of a qualified physician (or when appropriate, a qualified dentist). However, responsibility for medical care is not the same thing as responsibility for conduct of the clinical trial.

All investigational new drug research must have an FDA-approved study protocol. In the case of research supported by the pharmaceutical industry, the sponsor (company) designs the trial to generate safety and efficacy data needed to support appropriate labeling claims for the new product. Frequently, sponsors consult with expert scientists to assure that the study has scientific and clinical merit. Investigators are frequently asked for suggestions to improve the protocol, but the decisions on study design rest with the sponsor and FDA. The sponsor identifies and recruits investigators, who then have the right to agree or decline to participate in the study. The PI must submit his/her credentials on an FDA Form 1572 for approval by the sponsor and FDA.

Before a trial is initiated, the FDA requires the protocol to be approved by an institutional review board (IRB) or independent ethics committee. The IRB must address the investigator's qualifications to conduct the proposed trial. It does so by reviewing a current curriculum vitae and other relevant documentation. Pharmacists seeking approval by an IRB must demonstrate experience in the conduct of clinical trials similar to the one for which approval is being sought. The investigator provides information to the IRB, but does not participate in the committee's deliberations.

The FDA requires each PI to comply with GCP and other applicable regulatory requirements, permit monitoring and audits by the sponsor and the FDA, and maintain a list of qualified persons to whom the investigator has delegated

significant trial-related duties. A qualified PI must show familiarity with the compound to be studied and demonstrate adequate resources to conduct the trial. This includes being able to recruit in a timely manner an adequate number of subjects that meet protocol-defined entry criteria, have an adequate number of qualified staff, and have necessary facilities available for the anticipated duration of the trial. The PI is responsible for assuring that all staff assisting in the trial are well informed about the protocol, the investigational drug, and their duties with regard to the trial.

#### Responsibilities of the Investigator

##### General Responsibilities

A PI is responsible for the conduct of a scientific investigation in accordance with study methodology, a signed investigator agreement or contract with the sponsor (if applicable), and any federal or state rules and regulations regarding performance of a study using human subjects. The underlying premise is to protect the rights, safety, and welfare of subjects under the investigator's care and to control the distribution and use of drugs under study.

As mentioned, prior to initiation of the trial, the investigator needs IRB approval, an approved subject informed consent form, and approved subject recruitment procedures. The investigator must provide the IRB with current copies of the Investigator's Brochure for each investigational drug before beginning the trial, and must provide updated copies if the Investigator's Brochure is revised during the conduct of the study. The PI is accountable for obtaining written informed consent from all subjects. In life-threatening situations necessitating the use of the study drug, the IRB may approve other methods of obtaining informed consent. Regardless, an investigator may only obtain consent after a subject or his/her legally authorized representative has had sufficient opportunity to consider the risks and benefits of participation without coercion or unreasonable influence.

During the clinical study, a qualified physician or dentist, as appropriate, who is at least a subinvestigator must be responsible for all trial-related medical (or dental) decisions. The PI and the institution must ensure that adequate medical care is provided to subjects for any adverse events related to the trial. Intercurrent illnesses that are detected during the course of the study must be noted and the subject informed. If

agreeable to the study subject, the PI is also responsible for informing his/her primary physician about his/her participation in the trial. The investigator should make every effort to determine the reason for subject withdrawal from the trial, while being respectful of the subject's rights to withdraw without explanation.

During the performance of the study, the investigator must maintain adequate documentation of study activities and must promptly report any deviations from the protocol to both the IRB and study sponsor. Any changes to the protocol, all adverse drug reactions that are both serious and unexpected, and any new information that may affect adversely the safety of the subjects or their willingness to participate in the clinical trial must be promptly reported to the IRB. Substantive changes to the protocol must receive IRB approval. Investigators must also submit progress reports to the IRB at least annually; sponsors will usually request more frequent progress reports.

#### Investigator Record Keeping

The PI is responsible for maintaining records associated with the clinical study. These include case histories designed to record all observations or other pertinent data on each enrolled subject, independent of whether the subject received active treatment. Data for each trial subject is normally recorded on a case report form provided by the sponsor. The sponsor may also require study data to be recorded in a source document (patient chart). It is the responsibility of the PI to assure that the forms are filled out with the correct information and according to guidelines established by the sponsor.

Study drugs, whether investigational or commercially available, must be controlled and accounted for, and may only be administered to study subjects who have provided informed consent and who are under the supervised case of a trial investigator. Accordingly, a drug accountability log must be kept up-to-date and accurate. The log should record the disposition of the drug, including dates, quantity, and use by subjects. Study drugs must be secured in a locked storage area until destroyed, properly disposed of, or returned to the study sponsor.

Case histories, drug accountability logs, and all correspondence associated with the study must be secured and kept for 2 years after the marketing application is approved by the FDA. If no such application is filed, or if the application

is not approved by FDA, these records must be retained for 2 years after the investigation is discontinued and the FDA is notified. It is advisable that records from clinical trials supported by grants from academic, government, or voluntary health organizations also be maintained for this same time period, unless otherwise specified by the agency. If the study is part of an international clinical trial, or if specified by the sponsor, the PI may be required to keep a patient list with study drug assignments for 15 years after the conclusion of the trial.

In the case of premature termination or suspension of the trial, the investigator must promptly inform trial subjects, assure appropriate follow-up and treatment if required, and inform the IRB and regulatory authorities as appropriate. Similarly, when a trial is completed under normal conditions, the investigator must file final reports with the sponsor and inform the institution, the IRB, and regulatory authorities (as appropriate) that the trial is completed.

Finally, all records must be available on request from the FDA or study sponsor within a reasonable time. The authorized representative from the sponsor or FDA must be allowed to copy documents with patient identifiers omitted and must be provided sufficient time to verify records associated with the conduct of the study. Investigators are not required to provide the names of subjects unless the records of a specific individual require more intensive examination related to an adverse event, or there is suspicion that the records are falsified. Frequent or deliberate falsification of records may lead to disqualification of a PI to conduct future clinical studies, as well as potential criminal or civil prosecution.

#### Advice to Pharmacist Investigators

Before agreeing to participate in a sponsored clinical study, the PI should answer a number of questions about the logistics of conducting the protocol at his/her site and should create a sound plan for study implementation. To do so, the PI must understand the structure that governs research support and funding within his/her institution to avoid technical or financial problems during or after the study. Addressing the issues and questions identified in Figure 3 before starting the protocol will help in conducting a timely and successful study.

Once the PI agrees to participate in a clinical study, its successful initiation requires that the PI

have the following: (1) regulatory approval from the sponsor and FDA (if the study requires an Investigational New Drug application [IND]) through submission of FDA Form 1572; (2) legal approval by the investigator's institution of his/her contract and agreement with the study sponsor that details the scope of work, data ownership, intellectual property, publication rights, indemnification, and confidentiality; (3) budget approval from the institution's grants and contracts office; and (4) IRB approval of the study protocol and informed consent procedure. Investigators are encouraged to complete this process within 45 days to be competitive with other research service providers. Two major

pitfalls of which investigators must be aware involve budgetary planning and ownership of data. Poor planning in either regard can jeopardize the PI's ability to complete the project and disseminate new scholarly information (data ownership and publication).

### Budget

An essential component to any clinical trial is a well-planned budget that accounts for all resources and project costs. In many instances, the investigator will be competing with other sites for the research contract. Therefore, the budget must cover costs, provide a reasonable

## Study Logistics: Assessment and Plan

### I. Administrative Plan

#### a. Institutional approvals

- Determine if contract and investigator agreement regarding responsibilities, intellectual property, confidentiality, indemnification, data ownership, and publication rights are acceptable to your institution.
- Is approval needed from other institutional regulatory committees? This might include the radiation safety or biohazards committees.
- If the investigator is receiving funding for the study, how will these monies be handled within the institution? How much time is needed by the institution to set up the payment infrastructure?
- Does the institution have an overhead charge for government, voluntary organizations, or corporate studies? Will the PI have access to these excess monies after the study is complete?

#### b. IRB Logistics

- How often does the IRB meet?
- What are the requirements for submission of an IRB study packet?
- Take time to talk with the IRB personnel to understand the complete review process before submission. This will save time and prevent anxiety.

### II. Operational Plan

#### a. Physical Resources

- Where will the study be conducted?
- Does the study require an ambulatory care clinic, a clinical research center, or will patients need to be hospitalized? Use of these facilities will need to be negotiated with the institution.
- What types of tests are necessary? Laboratory testing, radiography, nuclear medicine, physical therapy, or other services should be contacted about the proper method of sending samples, ordering tests, and paying for services. Some institutions may offer research discounts for tests.
- How will the test data be collected? If study data are recorded in patients' charts or institution computers, will the investigator have access to these charts after the patient is discharged or the study is complete? Verification of records may occur several years after a study is complete; therefore, access to records must be confirmed prior to starting the study.

#### b. Human Resources

- Determine need for coinvestigator(s) and outline their roles.
- Determine need for study coordinator and responsibilities.
- Assign responsibilities and establish deadlines and milestones for all personnel closely related to the study (e.g., study coordinator, coinvestigators, research fellows).
- Visit with the nursing staff of the facility to avoid unnecessary delays in starting the protocol.

Figure 3. Recommended guidelines for assessment and planning of study logistics before conducting a study protocol.

incentive to the investigative team, and be competitive in the marketplace. All direct and indirect costs must be identified and negotiated among the PI, his/her institution, and the sponsor before initiating the study. In doing so, the PI will assure that the study can be completed and that useful information will be provided to all parties. The most commonly made error on the part of the PI is to underestimate study costs because of failure to identify all resources required to complete the study or to underestimate their true costs. As a result, the study may not be completed and/or the investigator's research program will not benefit from residual funds remaining in the contract budget after study completion. These monies can usually be used to sustain the infrastructure of the clinical facility or laboratory.

To avoid these problems, it is recommended that the PI consult with internal support staff knowledgeable in budget design and institutional overhead. Most academic centers have a clinical trials office that can help construct a comprehensive budget and provide accurate estimates on all institutional costs. If such an office does not exist, one can contact the campus grants and contract office or a peer group with experience in conducting clinical studies in the investigator's setting. Many times, the sponsor will generate a proposed budget for a trial based on usual and customary costs. These budgets are typically very complete, although they can be modified through negotiation with the sponsor if the increased costs can be justified.

The investigator must remember that most clinical trial budgets derived in academic settings must conform to the Health Care Finance Administration's corporate compliance regulations. The regulations state that federal health care payers are responsible for covering only those resources that are medically necessary for the care of a patient. Taxpayer dollars (e.g., Medicare) cannot be used to subsidize purely research activities, or for experimental or unproven medical therapies.

Research-related costs are derived from the investigator's hospital or clinic, laboratory testing or analysis, or through contractual arrangements with other laboratories. In addition, there may be patient recruitment costs such as advertising, patient expense reimbursement (parking and transportation), and participation honoraria. Research resources usually include equipment, supplies, and salary support for the PI and associated personnel. Salary support for the PI

and other study personnel generally has the greatest flexibility and provides an opportunity to generate residual funds to support the PI's overall research program.

From a financial perspective, the PI's primary objective when entering into a research contract is to complete the study successfully at or below the requested budget. The residual funds that result are often placed into a development fund on behalf of the PI and can be used at the investigator's discretion to support other research projects. Although this objective is perfectly reasonable, study expenditures and allocation of funds must be thoroughly documented throughout the course of the investigation. Accurate records are often requested by the sponsor, and occasionally by outside auditing agencies, and are essential to maintaining a productive clinical research program.

#### Publication Rights

A clear understanding of study responsibilities and publication rights should be negotiated among the PI, his/her collaborators, the study sponsor, and the investigator's institution prior to initiating the trial. It is best to involve all parties as early as possible and to negotiate all aspects before agreeing to the study contract. In this regard, most academic institutions have a liaison within their research office for business and industry contracts that can assist the investigator to organize and expedite this process. It should be the mission of the PI and liaison to ensure the investigator's freedom to publish the research findings. This includes the right to publish negative results. In doing so, the investigator has ownership of the data, materials, and documentation, but the sponsor receives copies and is given the right to use the materials for certain purposes. In general, sponsoring companies are aware of the research mission of academic institutions and are flexible in the negotiation process.

Any terms and conditions that restrict the publication rights of the investigator are usually reserved for the protection of the sponsor's patent rights that may arise from the contracted work. In this situation, the sponsor is granted a specified period of time (e.g., 30 days) to review the proposed publication before its submission and is provided the right to withhold publication for a specified time period (preferably no more than 90 days), pending submission of a patent application. It is always important to identify in

the contract that the investigator and supporting institution will not allow any publication restriction in such a way as to impede the academic progress of a graduate student or research fellow if these individuals were integrally involved with the study. If any publication restrictions are accepted on behalf of the PI and students, they should be agreed to in contractual form before initiating the trial.

Finally, in single-center trials, the order in which authors are listed on the publication is usually the responsibility of the investigators involved with the study. Therefore, choose collaborators wisely. In multicenter trials, the publication rights of individual investigators and the expeditious publication of results become more complex. In this case, the investigator must accept the risk of sacrificing both ownership and timely publication of research findings despite a priori agreements with the study sponsor. Many sponsors choose authors for multicenter studies based on the reputation of those authors in the area of study or based on the number of subjects that their site enrolled in the trial. Thus, younger investigators, or investigators from smaller study sites, may find themselves excluded from the publication process.

### **Qualifications of a Successful Principal Investigator**

It is important to emphasize that even though pharmacists may serve as PIs for industry-sponsored clinical research, the mere fact that a person is a pharmacist does not automatically qualify him/her to serve in this capacity. An investigator must establish his/her qualifications and credentials before he/she can reasonably expect an industry sponsor to trust him/her to serve as PI.

#### **Experience**

A PI typically evolves from a subinvestigator. Although we may consider our research trainees ready to assume a career as an independent scientist on completion of their program, 2–3 years of postdoctoral research training may not realistically provide them with sufficient experience. For example, a qualified PI should have relevant clinical experience in the proposed study population, usually gained from several years of experience in patient care. However, this patient care experience alone does not automatically qualify someone as an investigator. Understanding and demonstrating competence in

clinical research practices, demonstrated compliance with research regulations and data management, and the ability to create and manage an investigational plan through task delegation must also be considered.

#### **Local Resources**

The PI must demonstrate that he/she has acceptable and adequate resources available to manage the trial, including access to or control over clinical space such as beds and clinics, if needed. The facilities must have appropriate staff and other resources to conduct the research and to protect the subjects. Specialized testing equipment needed for the experiments must be available, either in the form of general testing purchased from the health system or in the PI's own laboratory.

#### **Command of the Research Process**

The PI must be knowledgeable about the multiple processes needed to manage a clinical study, including the medical records system, investigational drug pharmacy, clinical laboratory, other clinical departments necessary to support the project, the institutional review and approval processes, budget and financial management, and contract initiation.

#### **Human Resources**

The PI must generally demonstrate the existence of a qualified research and clinic staff, as appropriate. Very few studies can be managed by a single individual, and PIs have many other responsibilities. Thus, a successful PI must be able to delegate responsibility and hold other people accountable.

#### **Access to Patients**

An industry sponsor is very keen on knowing that the PI can enroll and complete the number of patients required or requested in a contractual agreement. The sponsor's research and business plans are entirely dependent on productive and enthusiastic PIs and study coordinators. Some pharmacists may be limited in identifying and enrolling study subjects by having insufficient direct professional responsibility for patient management, or by having access to patients only through physicians. To overcome this potential limitation, the PI should demonstrate the ability to recruit qualified patients through advertising or similar means.

## Audits

Proof of competence is an increasing demand. Principal investigators must be able to show they have the ability to perform in compliance with research regulations through outside audits of process and product. The ability to demonstrate this competence through a portfolio of projects, meeting contractual obligations, and generating good data will serve as an effective reference for obtaining recognition as a PI.

## Local Leadership and Environment

The leadership of local pharmacy organizations (e.g., colleges of pharmacy, departments of pharmacy, academic medical centers) must be supportive and encouraging, must remove barriers to successful research, and must encourage multidisciplinary collaboration permitting pharmacists to reach their potential. These local leaders can play a great role in promoting their new members into a career in clinical research and providing an environment conducive to this endeavor.

## Conclusions

Clearly, an individual's academic degree alone does not imply that he/she possesses adequate skills and experience to serve as a PI. The FDA

and pharmaceutical industry are aware that pharmacists can be excellent investigators. However, as is the case with any PI, the pharmacist must have a proven track record that demonstrates successful clinical trial management. As outlined above, serving as PI is an arduous task. There are many responsibilities that require the investigator to adhere to local institution, industry, regulatory, and human assurance guidelines and policies. Adherence to these guidelines requires extensive documentation. In addition, the investigator must enroll patients, execute the protocol, and meticulously collect and report patient data. Given these responsibilities, it is understandable why the industry sponsor needs to select PIs carefully. It is the opinion of the ACCP that the pharmaceutical industry should support policies and practices that use clinical pharmacists as PIs, as long as the pharmacist is an experienced clinical researcher with documented credentials, has the adequate institutional infrastructure and support, and has access to the required patient population.

## References

1. American College of Clinical Pharmacy. Clinical pharmacists as principal investigators. *Drug Intell Clin Pharm* 1983;17:675-6.
2. American College of Clinical Pharmacy. Clarification regarding clinical pharmacists as principal investigators. *Drug Intell Clin Pharm* 1984;18:444.

### ACCP Abstract Correction

The abstract below was presented at the 2000 Spring Practice and Research Forum of the American College of Clinical Pharmacy, April 2-7, 2000, at the DoubleTree Hotel in Monterey, California. It was inadvertently designated as an encore presentation when published in the March 2000 issue of *Pharmacotherapy*. The complete abstract consists of original research that has not been published previously.

**23. In vivo effect of antisecretory agents on immunomodulation and T-lymphocyte proliferation.** Jill A. Rebeck, Pharm.D., Kimberly L. Bergman, Pharm.D., Samuel J. Pirruccello, M.D., Keith M. Olsen, Pharm.D.; University of Nebraska Medical Center, Omaha, NE.

**PURPOSE:** The proposed mechanism of immunomodulation among antisecretory agents is related to enhancement of CD<sub>8</sub> (T-suppressor cell) activity. This study compared the effects of omeprazole and ranitidine on lymphocyte number, subsets, and proliferation in healthy volunteers.

**METHODS:** Seven healthy subjects (five males/two females; mean age: 30.6 ± 6.8 years) were randomized in cross over fashion to seven days of omeprazole 20 mg/day or ranitidine 150 mg twice/day followed by ≥ 1-week washout between treatment arms. Peripheral blood mononuclear cells (PBMC) were isolated and counted at each timepoint. Lymphocyte proliferation assays were performed with phytohemagglutinin for 72-hour stimulation, with <sup>3</sup>H-thymidine incorporation during the final 6-hour incubation. Treatment arms were compared to baseline regarding lymphocyte counts, flow cytometry analysis (markers included CD<sub>3</sub>, CD<sub>4</sub>, CD<sub>8</sub>, CD<sub>19</sub>, CD<sub>56</sub>, and HLA-DR), and <sup>3</sup>H-thymidine uptake (disintegrations per minute).

**RESULTS:** Baseline mean ± SD lymphocyte cell counts (in millions) were 33.9 ± 12.9, compared to 39.7 ± 15.0 and 34.9 ± 14.4 after omeprazole and ranitidine therapy, respectively (p>0.05). The mean CD<sub>4</sub>/CD<sub>8</sub> ratio was 2.79 at baseline compared to 2.67 and 2.57 for omeprazole and ranitidine, respectively (p>0.05). The percentage of T-suppressor cells did not change during any phase of the study. <sup>3</sup>H-thymidine uptake following omeprazole and ranitidine therapy was 30.9% and 5.8% below baseline values, respectively, compared to a 78% increase above baseline upon medication discontinuation (p<0.001).

**CONCLUSIONS:** A significant trend toward enhanced immunomodulation effects was seen with omeprazole and ranitidine therapy, as measured by T-lymphocyte proliferation. These findings suggest an alternative mechanism is responsible for immunomodulatory actions of the antisecretory agents.