

Development of a Clinical Pharmacology Graduate Program at the University of Kentucky

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This paper presents a summary of the philosophy, mechanism and possible outcomes of a graduate program initiative at the University of Kentucky College of Pharmacy. The program is intended to develop pharmacy trained specialists who independently will derive new knowledge through observation, study and experimentation that is focused on drug therapy outcomes in patients, and the factors and mechanisms determining those outcomes. Successful completion of this "Clinical Pharmacology Program" would ultimately lead to the PhD degree in Pharmaceutical Sciences, the umbrella graduate program at the University of Kentucky College of Pharmacy. This program is designed for individuals holding the PharmD degree who are interested in a rigorous, mechanistic approach to problems in clinical pharmacology and in establishing themselves as independent scientists through: intense clinical experience in a medical specialty of interest, state-of-the-art course work, and integrated laboratory-based and clinical dissertation research. It is emphasized that this program will continue to evolve in response to institutional and disciplinary needs and opportunities.

INTRODUCTION

The need for pharmacy to develop clinical pharmaceutical science training programs has been recognized since the Millis Commission published its 1975 report on "Pharmacists for the Future"(1). The term "clinical scientist" was simply described in that report as an individual equally skilled and trained in both the practice and science of pharmacy. Although the Millis Commission effectively articulated a societal need for such highly trained individuals, pharmacy academic institutions have made limited progress in developing programs to train "clinical scientists".

Hesitancy to develop such programs is multifactorial. First, the term "clinical scientist" means different things to different people. These differences will manifest varied answers to the following fundamental questions: What unique contribution will this individual make to the biomedical research environment? What unique knowledge base and experiential (laboratory and clinical) skills will this individual need to be successful in biomedical research? What mechanism(s) should be utilized to effectively and efficiently train these individuals for their career in research? In what environment (*e.g.*, laboratory or clinical, academic or industrial) will these new scientists eventually function? How will the profession, academia and society at large benefit from individuals trained in this manner? Despite the lack of a national pharmaceutical science consensus on these most important issues, institutional consensus should be easier to achieve. However, colleges of pharmacy have made limited progress toward the development and imple-

mentation of such programs(2). This may be attributed to the high cost of implementing these programs. Certainly, the difficulty in obtaining new state and industrial support for such new initiatives represents a real challenge in today's economic climate. Consequently, new graduate programs must compete with existing graduate programs for institutional resources. Also, the lack of a critical mass of faculty committed to the training of these unique graduate students may represent an additional problem for program development.

In 1986, the University of Kentucky College of Pharmacy introduced a new graduate program initiative intended to recruit pharmacy graduates into a program designed to develop independent specialists who will derive new knowledge through observation, study and experimentation that is focused on drug therapy outcomes in patients, and the factors and mechanisms determining those outcomes. This program would ultimately lead to the PhD degree in Pharmaceutical Sciences (umbrella program at the University of Kentucky College of Pharmacy) and has been identified as "Clinical Pharmacology Program". This paper details a summary of the philosophy, mechanism and possible outcomes of this program.

PROGRAM OVERVIEW

The philosophy of the "Clinical Pharmacology Program" at the University of Kentucky College of Pharmacy is predicated on the premise of a societal need for pharmaceutical scientists who possess broad clinical knowledge and experi-

ences coupled with strong analytical and problem solving skills in the area of applied biomedical research. Although there exist no objective data describing this need, we believe based on inquiries from colleagues in academia, industry and government that such a need truly exists. Further, the Millis Commission(1) and several pharmacy professional organizations(3-5) have emphasized the need for the development of such programs.

This program's main focus is in the area of applied pharmacology and experimental therapeutics. This area naturally evolved as a consequence of the critical mass of college clinical and basic science faculty with strong research interests in experimental therapeutics. Other equally important but distinctly different areas of emphasis (e.g., pharmacoeconomics and pharmacoepidemiology) presently are not included in this program. The program is administered from the Division of Pharmacology and Experimental Therapeutics with guidance from a steering committee composed of representatives from the Division of Pharmacology and Experimental Therapeutics and the Division of Pharmacy Practice and Science. Participation of faculty from both divisions and other faculty members from the College and Medical Center has been an essential component of the evolution of this program. The program requires the PharmD degree as a prerequisite for admission and attempts to build from this strong clinical foundation. The program is composed of extensive graduate level didactic course work with a strong biological science emphasis. Thesis projects require integration of clinical and laboratory skills directed toward the pursuit of knowledge relevant to problems in contemporary pharmacotherapeutics. The program meets or exceeds all college and graduate school requirements for the PhD degree.

Program Educational and Training Objectives

The objectives of the Clinical Pharmacology Graduate Program is to train independent scientists to conduct research in clinical pharmacology through:

1. intense clinical experience in a medical specialty of interest (examples include: cardiology, critical care, neonatal/pediatric medicine, neuroscience, and pulmonology);
2. state-of-the-art coursework in cell and molecular biology, pharmacokinetics/dynamics, drug metabolism and disposition, statistics, and;
3. integrated laboratory-based and clinical dissertation research.

Program Structure

The College of Pharmacy is one of five health science colleges associated with the University of Kentucky Medical Center. The College of Pharmacy is organized into three academic units (divisions): Medicinal Chemistry and Pharmaceutics (physical and chemical sciences); Pharmacology and Experimental Therapeutics (biological sciences); and Pharmacy Practice and Science (clinical, social and economic sciences). Some overlap occurs between divisions and contributes favorably to collaborative efforts across divisional lines. This is best exemplified by the fact that many Pharmacy Practice and Science faculty possess strong interests and skills in the biological sciences particularly as it relates to research in clinical pharmacology and pharmacotherapy.

The college administers one graduate degree program

under the general descriptor, PhD Program in Pharmaceutical Sciences. Historically, the majority of our graduate students completed their studies in the emphasis areas of medicinal chemistry or pharmaceutics (i.e., pharmacokinetic, physical pharmacy). The addition of a strong graduate program in pharmacology provides our college with a unique opportunity to train graduate students in both the physical/chemical or biological sciences. The Divisions of Medicinal Chemistry and Pharmaceutics, and Pharmacology and Experimental Therapeutics are responsible for supporting their own graduate initiatives. The Clinical Pharmacology Program is currently administratively organized in the Division of Pharmacology and Experimental Therapeutics. The rationale for this alignment will be discussed below.

The graduate program within the Pharmacology and Experimental Therapeutics Division offers two different options toward pharmacology graduate education: (i) "basic science", and (ii) "clinical science". At this time, the Pharmacology and Experimental Therapeutics Division supports graduate studies in three distinct areas of emphasis: neuropharmacology, cardiovascular pharmacology, and pharmacokinetics/pharmacodynamics and drug metabolism. These three areas of emphasis reflect the existence of a critical mass of faculty functioning within these areas of concentration. They also reflect existing strengths and interests of experimentally oriented faculty in the Pharmacy Practice and Science Division. The Clinical Pharmacology Program Steering Committee is charged with overseeing the continued development of the program, particularly as it relates to program quality and structure. The collaborative effort of both divisions has resulted in true synergism.

The decision to place this graduate program in the Pharmacology and Experimental Therapeutics Division was based on a number of institutional considerations. Originally, the program was conceived outside of a particular academic unit with faculty from all divisions contributing to the support and guidance of this initiative. This was possible because of our divisional versus department structure. However, it soon became apparent that the program would need to be aligned with an academic unit in order to receive its share of institutional resources. It was generally believed that the Pharmacology and Experimental Therapeutics Division, which includes the areas of pharmacokinetics and pharmacodynamics was in the best position to initiate this program. This decision was made in conjunction with faculty in the Pharmacy Practice and Science Division but not without considerable constructive debate. Many detractors would argue that a "Clinical Pharmacology Program" should be housed in a clinical academic unit.

This concern legitimately raised the questions of program participation and ownership. However, we were more concerned with program implementation and there were a number of reasons not to place this program in the Pharmacy Practice and Science Division. First, all PhD programs (including those within the College of Medicine) at the University of Kentucky are directed out of basic science units. Second, most of the clinical faculty interested in participating in this program were at the assistant professor level and only beginning to develop their clinical research programs. Third, full graduate faculty status was limited to only a few clinical faculty at that time resulting in the lack of a "critical mass" of graduate level faculty to support such a program. Fourth, research resources (project funds, equipment, laboratory space etc.) for our faculty engaged in

clinical research are currently limited. Fifth, most clinical faculty believed that an integrated approach (basic and clinical faculty working together) would provide clinical faculty with the opportunity to become significantly involved in the program and evolve into full participation. It should be noted that there exist few graduate trained faculty in clinical science units within colleges of pharmacy. It is hoped that programs like this one will address this concern. In addition, clinical faculty were not originally hired to provide support for or develop graduate level programs. In the past, clinical faculty have contributed greatly to clinical scientist training by directing post-PharmD residency and/or fellowship programs. It is expected that by working with basic science colleagues with similar therapeutic interests all will gain from the experience. This program is not accomplishable without the joint participation of these two academic units.

Program Components

The wisdom of bringing the physical/chemical sciences into the pharmaceutical sciences in the early 1950s resulted in the emergence of two major research disciplines, Medicinal Chemistry and Pharmaceutics. As a result, the development of strong graduate programs in these areas occurred where College and University strengths and priorities were directed toward the physical and chemical sciences. These programs have long served as the intellectual cornerstones of colleges of pharmacy. The development of these highly competitive, internationally regarded medicinal chemistry and pharmaceutics programs would not have been possible without effective institutional cooperation. Similarly, graduate programs in the clinical pharmaceutical sciences will require special institutional strengths in order to blend a strong graduate level biological science laboratory base with extensive clinical research activities. The development of such a program at the University of Kentucky College of Pharmacy was viewed possible as a consequence of such favorable institutional characteristics.

The College of Pharmacy is administratively and physically associated with the University of Kentucky Medical Center. We believe that such an association is important and brings together a critical mass of faculty or collaborators in a focused area of therapeutic emphasis. The College has enjoyed a strong local and national reputation in graduate education and research. In addition, the College has been a pioneer in clinical pharmacy education and residency training programs dating back to the late 1960s. Clinical and basic science faculty within the college have enjoyed a viable, highly productive collaboration particularly in the area of experimental therapeutics. The opportunity to interact with faculty outside our college, particularly clinical and basic science faculty from the College of Medicine, has further enhanced our opportunities to pursue multidisciplinary approaches toward problem solving.

Initially, interests in the general area of pharmacokinetics and pharmacodynamics served as the common thread linking clinical and basic researchers. This was a natural association since the tools of pharmacokinetics and pharmacodynamics could easily be applied to problems in clinical pharmacy and pharmacology. Although pharmacokinetics and pharmacodynamics research remains an integral component to our Clinical Pharmacology Program training program, faculty focus primarily on disease state priorities. The blending of clinical and basic science ap-

proaches toward solving disease oriented problems relevant to the pharmaceutical sciences has been encouraged institutionally through the development of research centers (*e.g.*, Center for Geriatric Research, Cancer Center, Center for Cardiovascular Disease) as well as by priorities at the NIH. The development of these University based research centers has provided our faculty and students in this program with excellent access to complementary physical and intellectual resources.

As with any new graduate program, the source of a critical mass of scholars needed to support and mentor students will be heterogeneous. This characteristic will change with time as colleges prospectively hire faculty with training backgrounds and experiences more compatible with the philosophy and unique training needs of the program. Currently, we utilize faculty with backgrounds in basic pharmacology, pharmacokinetics, pharmacodynamics, drug metabolism, molecular biology and clinical pharmacy. In addition, graduate students in this program require a critical mass of students and postdoctoral students who share commonality in background and purpose while possessing some scientific diversity. These faculty and student critical mass issues are important since the learning and challenges which takes place in the laboratory or clinical settings, discussions groups, or departmental seminars are vital components to the training of a graduate student. We believe most of these environmental elements are critical to the successful development of a Clinical Pharmacology Program and are necessary for the development of a fertile intellectual environment.

Program Description

Prerequisites. Following considerable discussion and debate, it was decided that the PharmD degree would be a prerequisite for admission to the Clinical Pharmacology Program. This decision was made in lieu of a combined PharmD-PhD degree for several reasons. First, we did not believe it possible for a student to assimilate a meaningful professional and graduate didactic and experiential component within the framework of a single program. It has been suggested that we must "fast track" students through their professional program in favor of capturing them in the graduate program. This concept would be reasonable for most research areas of interest such as traditional pharmaceutics and medicinal chemistry programs. However, we believe that students pursuing a career interest in clinical pharmacology must have a full complement of clinical didactic and experiential elements prior to advanced studies at the graduate level. Second, as an increased number of entry-level PharmD graduates are produced, a graduate program with the PharmD degree as a prerequisite would prevent unnecessary duplication of experiences. We want our students entering this graduate program to have a strong clinical perspective as well as a solid foundation in the areas of pathophysiology and advanced therapeutics. This program will build further upon this strong clinical foundation. We recognize that this prerequisite will temporarily disadvantage us in the recruitment of quality BS students with interest in this program.

At the present time our recruitment goals are modest with no more than two or three students entering the program per year. This prerequisite has not been problematic. We have had considerable success in recruiting quality PharmD students not only from our own program but from

out of state as well. In addition, as more colleges of pharmacy move toward entry-level only PharmD programs, the best students are likely to want to differentiate themselves. We expect that graduate level clinical science programs will be attractive to these students.

Graduate "Residency" Requirement. Since July 1, 1992, all students entering the Clinical Pharmacology Program have been required to spend much of their first year in a clinical graduate "residency" experience. This requirement is intended to provide the student with an opportunity to work closely with members of our clinical faculty within an area of the student's research interest. This will provide the student with the opportunity to: (i) strengthen his/her perspective of clinical problems within this research interest area (e.g., cardiovascular pharmacotherapy); (ii) establish important relationships with clinical faculty from both the Colleges of Pharmacy and Medicine; and (iii) actively participate with a member of our clinical faculty in their clinical research program. This student is not expected to perform a significant service function to the institution but rather use this opportunity to nurture his/her knowledge in therapeutics and perspective of clinical research.

It is anticipated that this experience would aid the student in the development of a clinically oriented thesis project. Furthermore, the student will continue to apply the clinical skills developed during the first year to his/her research focus throughout the entire training program. Another positive consequence of this activity will be the opportunity it will create for participating members of our clinical faculty. The opportunity to have significant interaction with a graduate student during his/her first year will enhance our clinical faculty's chances for full participation in the program. During the first year, the student will also begin taking core course requirements (see below).

Didactic Requirements. A considerable amount of flexibility exists in the course work requirements of all students enrolled in our graduate program. Course requirements for each student's program are set by graduate faculty within the Division as well as the students advisory committee. Consequently, no two students are likely to have the same course requirements. The total number of didactic hours ranges from 50 to 60 depending on the individual student. As with most graduate programs, the advisory committee plays a vital role in determining these requirements based on the needs and interests of the student. This combination of minimum structure and maximum flexibility is particularly important with this Clinical Pharmacology Program. A need presently exists to expand course offerings for students in the Clinical Pharmacology Program. The following represents a summary of course offerings for students in the Clinical Pharmacology Program.

Core. The core curriculum is designed to provide students in this program with a broad background in biochemistry, physiology, advanced pharmacologic concepts, pharmacokinetics/pharmacodynamics, drug metabolism, pharmacotherapy and statistics. These areas have been identified by the Clinical Pharmacology Steering Committee as crucial to the development of a contemporary biologically oriented clinical scientist. Consequently, graduate level course work in each of these subject areas is required of all students in the program. In addition, advanced graduate level courses are selected by the student (see below) de-

pending on pharmacotherapeutic or research area of interest.

Electives. Elective course work is available in the areas of biochemistry, pharmacology, pharmacokinetics and drug metabolism, toxicology, physiology, and statistics. Since biochemistry is considered an essential building block to a scientific career in the biological sciences. Students in this program typically take a minimum of three additional semesters of biochemistry (8 credits)/molecular biology (2-4 credits). In addition, a summer "hands-on" molecular biology laboratory course is recommended for those students who anticipate using these techniques in their research project. Most students select a graduate level analytical course (4 credits) which provides both theoretical and laboratory experiences. Additional electives are selected on the basis of student strengths and weaknesses as well as their area of interest (e.g., pharmacokinetics and drug metabolism, cardiovascular clinical pharmacology, neuro-clinical pharmacology, etc.)

Assistantships. Students serve as teaching assistants and research assistants. During their first year, they are also involved in clinical clerkship teaching.

Dissertation Requirement. A "significant" component of the student's dissertation project must involve a clinical component. This requirement is difficult to articulate because no two projects are alike. The determination of what constitutes a significant amount of clinical work will be left to the discretion of the advisory committee and Clinical Pharmacology Steering Committee. It is expected that most students will utilize classic clinical pharmacology, animal laboratory, as well as contemporary analytical and molecular biology tools to address specific aims within their dissertation proposal.

Clinical Pharmacology Steering Committee. The Clinical Pharmacology Steering Committee is appointed by and reports to the Director of Graduate Studies. The purpose of this committee is to provide a broad overview of the Clinical Pharmacology Program. The Committee includes members from both the Division of Pharmacology and Experimental Therapeutics and the Division of Pharmacy Practice and Science as well as other faculty members from the College and Medical Center who are involved in this program.

Student Advisory Committee. The student advisory committee within the Clinical Pharmacology Program functions in an identical manner to other graduate advisory committees within our College and University. However, it is required that at least one member of the Pharmacy Practice and Science Division be a part of the student's core committee. It should be noted that graduate faculty status within our university and college is attained through the following process: (i) A member of the faculty (basic or clinical) applies to the graduate school through the Director of Graduate Studies within the College of Pharmacy. The faculty member's C.V. along with a letter of support from the college's Director of Graduate Studies is forwarded to the Graduate School for consideration; (ii) If approved, the faculty member is given an Associate Member appointment in the Graduate Faculty which affords him/her the privilege of co-advising students or participating on a student's graduate committee; (iii) Once the faculty member is promoted to Associate Professor, he/she becomes eligible to indepen-

dently direct graduate student research. Currently, there exists no differentiation between basic and clinical science faculty.

CAREER OPPORTUNITIES

A new academic program must be justified on the basis of a societal demand for its product. Pharmacy based graduate programs in the Pharmaceutical Sciences have provided our students with excellent career opportunities within the pharmaceutical industry, government agencies, as well as academic settings. Career opportunities in these settings are beginning to develop for pharmacy based graduate level trained "clinical scientists" possessing research skills which integrate clinical and basic sciences.

To date, post-PharmD fellowship training programs have been the primary supplier of clinical scientists for the pharmacy profession. Although products of these programs have made significant contributions to biomedical research over the past 10 to 15 years, we believe that programs like our Clinical Pharmacology Program will offer students numerous career advantages. Although there currently is strong interest in our students from various job market sectors, it is our hope that a large percentage of our graduates will find a home in clinical academic units of colleges of pharmacy. Their pharmacy background, strong clinical knowledge base coupled with clinical and teaching experience and demonstrated ability to integrate clinical and basic science research tools toward the solution of contemporary biomedical problems make them ideally suited for academic careers. In order for this to occur, colleges of pharmacy will have to reconsider the structure and function of clinical units. For example, most clinical faculty positions carry a large percentage of didactic and clinical instruction as well as a significant amount of patient care responsibilities. Although these job responsibilities are vital to our teaching and service programs, we must create career opportunities for a modest number of "clinical scientists" within these units. Such a commitment would include the provision of appropriate laboratory facilities and start-up funds traditionally reserved for our basic science faculty. Otherwise, our graduates will migrate to traditional basic science units or to the pharmaceutical industry where they may be afforded the infrastructure support to launch their professional career. This new clinical faculty member would be expected to compete at a comparable level to traditional "basic science" faculty for competitive as well as noncompetitive extramural funding.

FUNDING

As mentioned earlier in this manuscript, a critical question in need of addressing will be the funding of these programs. Attracting quality students into these programs will require

a substantial amount of support. Because of the nature of these students' projects (*i.e.*, a blend of clinical and laboratory experiences), project cost tends to be higher than that of traditional graduate students. Consequently, programs and individual faculty advisors will require a significant amount of research support. Since these students have a PharmD degree we are often competing with residency and fellowship stipends which are frequently two times higher than stipends afforded our graduate students. This fact alone has discouraged some very interested students from pursuing our program. Graduate students in this program have the potential to make a substantial contribution to our teaching program because of their strong pharmacy based backgrounds. Consequently, they may be deserving of additional financial support.

Funding of training programs is principally the responsibility of the institution and the individual faculty. A challenge for pharmacy is to effectively convince government agencies (*e.g.*, NIH and FDA) to recognize the PharmD degree as an appropriate precursor for graduate education in the area of clinical pharmacology. In addition, pharmacy must lobby hard for the opportunity to compete for postdoctoral NIH training grants in clinical pharmacology. In light of the growing societal concerns regarding manpower shortages in the discipline of clinical pharmacology, programs like ours may be a reasonable complement to existing MD/PhD programs in clinical pharmacology.

SUMMARY

This paper describes a graduate program initiative at the University of Kentucky College of Pharmacy. Specifically, the Clinical Pharmacology Graduate Program seeks to train individuals who will be conversant with clinical problems and yet be able to function as independent investigators in a laboratory setting. A description of the philosophy, mechanism and potential outcomes of the program is provided.

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