

“Clinical Pharmacology: A Retrospective View of the Future”

The discipline of clinical pharmacology has had a long and well chronicled history. Logarithmic growth of the discipline occurred concurrent with the therapeutic explosion of the 1950's in the United States. The Kefauver-Harris Amendments to the new drug approval process in 1962 ignited the field by requiring efficacy data on all new NDA submissions. During the decade of the 1960's, a number of clinical investigators with differing backgrounds ranging from basic sciences to medicine participated in the structure and execution of clinical drug evaluation.

Concurrent with the increased interest in the discipline, Dr. Harry Gold, along with Dr. McKeen Cattell, and Dr. Nathaniel T. Kwit, clinicians, researchers, and teachers from Cornell Medical College in New York City, organized the American College of Clinical Pharmacology and Chemotherapy (ACCPC), the forerunner of the American College of Clinical Pharmacology (ACCP), in 1963. Dr. Alphonse Ingenito's 25-Year History of the American College of Clinical Pharmacology, written in October 1994, related that prominent roles in recruiting members and developing the new organization were also played by Drs. Duncan E. Hutcheon and Theodore Greiner. Dr. Hutcheon identified a need for an organization primarily devoted to increasing knowledge and developing high standards for the merging discipline of clinical pharmacology as it related to drug therapy, and to serve the needs of many diverse workers in the field; those with varying biomedical degrees, training and background who shared a common interest in the basis for rational drug therapy. At about the same time, Dr. Benjamin Calesnick, a clinician, teacher and researcher at Hahnemann Medical College in Philadelphia, foresaw a great need for qualified, well-trained investigators. He wrote a proposal for such training which included a suggestion for board certification in clinical pharmacology, and corresponded with many established pharmacologists, particularly members of the American Society for Pharmacology and Experimental Therapeutics (ASPET) to determine their reaction to the proposal. Dr. Calesnick was recruited into the new organization. The ACCPC eventually merged with the

American Therapeutics Society (ATS), a large group of physicians, with the original identified purpose of “the study and advancement of therapeutics.” A section from Dr. Ingenito’s history states:

“ One surmises that the early founders of ACCP were among those opposed to this merger. Reasons for this opposition were later explained in a 1971 editorial in the *Journal of Clinical Pharmacology* by Harry Gold. Gold made a distinction between clinical pharmacology on the one hand, and therapeutics on the other. He stated that clinical pharmacology is drug- oriented while therapeutics is patient-oriented. He regarded them as entirely different disciplines, which, while interdependent, differ in many respects, including training. He explained that while clinical pharmacology deals with the science of how drugs act, their toxic effects, pharmacokinetics, metabolism, etc., therapeutics concerns itself mainly with controlling the disease process in a practical sense. The main functions of ATS were determined to be sufficiently divergent from those of ACCPS, according to Gold, to originate ACCPC in 1963, and to resist later attempts to merge them.....The two societies eventually did merge, in December 1969, and adopted the name American Society for Clinical Pharmacology and Therapeutics (ASCPT), which exists as such today. Some within ACCPC who opposed the merger subsequently formed the present American College of Clinical Pharmacology (ACCP) in 1969.”

The American College of Clinical Pharmacology was composed of individuals with doctoral degrees from varying backgrounds, with medical (M.D.) and or doctor of philosophy (Ph.D.) degrees being most prominent. In that same era, Dr. Duncan Hutcheon predicted that there would be a “specialty board for clinical pharmacology created by 1977.”

On August 5, 1976, the American Board of Clinical Pharmacology (ABCP) was incorporated as a non-profit organization by Dr. Duncan Hutcheon. The first organizational meeting of the ABCP was held on April 28, 1978, and basic concepts of board examinations were discussed for further development. Six subsequent meetings were held in 1978, and the first

examination dates were set for May 1 and 2, 1979. Subsequently, delays for the examinations were called for by the ASCPT and ASPET, which also requested the formation of a “Tripartite Task Force” to review the exam process. This Task Force was reorganized as the Council of Clinical Pharmacology on June 19, 1981, and negotiations for the Council to sponsor the ABCP began, but never materialized. From 1982 through 1986, series of discussions concerning the certification process were held. Due to the inability of the Council to sponsor the original legally incorporated Board from Dr. Hutcheon, in 1986, the Regents of ACCP agreed to acquire the ABCP. In 1987, there was agreement to give the Board exam in the spring of 1988. The Council was formally disbanded in March 1988, and an independent Board was transformed from it. Dr. Alexander Shepherd was appointed Chairman of the new free-standing Board, with six representative members serving from each of the three societies, ACCP, ASPET and ASCPT. The first exam was held on May 19, 1991. Controversy over non-MD certification persisted, and in 1991, the ACCP Regents officially supported a single certification by the Board for all doctoral applicants, non-M.D.’s as well as M.D.’s.

As the American Board of Clinical Pharmacology evolved, distinctions were made between doctoral background such that separate exams in clinical and applied pharmacology were proposed. Because of this structure, the Board of Regents of the American College of Clinical Pharmacology elected to develop this white paper on the future role of clinical pharmacology for the next millennium.

Because of both the history of the discipline and the diversity of its practitioners, a clinical pharmacologist is a person with a doctoral degree, who is actively and persistently involved in activities pertaining to optimizing therapeutics. The College believes that the doctoral degree may rest in either the clinical or basic science disciplines related to the health sciences. The rationale for this acceptance of diversity in the conduct of clinical pharmacology research rests in the changes that have occurred in health care delivery over the course of the past two decades. At this point in time, individuals from various backgrounds are actively involved in patient care, oftentimes under the umbrella of legally sanctioned collaborative practice

opportunities. Furthermore, the expertise brought to the discipline by individuals in specific scientific areas, such as molecular biology, proteomics, biostatistics and pharmacokinetics / pharmacodynamics, make their knowledge essential to the conduct of research in both today's and tomorrow's therapeutic evaluation. These individuals may participate in the discipline in various locations, including university medical centers, various ports of health-care delivery in our society, those industries related to the development of new therapeutic entities, legal and regulatory agencies, and other private practice or consultant venues. As far back as the late 1960's, there has been a clear need for improved utilization of drugs in our society. In the late 1960's, researchers identified approximately a \$1 - \$3 billion cost to society associated with the inappropriate use of drugs. In the mid-1990's, a study placed the cost of therapeutic misadventuring at \$76 billion. Clearly, this continuing problem indicates a need in society for optimized drug therapy and the development of specialized knowledge in the area of therapeutics. It is important for individuals with expertise in clinical pharmacology to become involved in the therapeutic process as early as possible. In this manner, it is our belief that patients can receive optimal care related to their therapeutics experience. In addition, continual monitoring of drug therapy is essential for the optimization of therapeutic response, which is the ultimate goal of the discipline of clinical pharmacology.

The intellectual content of the discipline ranges from basic principles of pharmacokinetics and pharmacodynamics to the design and execution of clinical drug trials. Individuals involved in the discipline should have training in molecular mechanisms of drug action and toxicity, pharmacoepidemiology, pharmacogenetics, medical ethics, human pharmacology, and regulatory pharmacology and drug development. Individuals equipped with this background conduct research ranging from molecular pharmacology to human pharmacology, with an ultimate goal of identifying the mechanisms and consequences of drug action. Once identified, these principles are translated into clinical therapeutics with an eye towards optimal therapeutic response. The specialized knowledge that results from clinical pharmacology studies should be applied to the everyday evaluation and treatment of patients

with clinical problems related to all aspects of drug therapy. In addition, it is our belief that clinical pharmacologists have a responsibility for imparting the knowledge gained in the discipline and the principles of human pharmacology to future trainees in the healthcare disciplines.

Because of the diverse nature of the field, it is believed that there are at least two distinct areas associated with the development of new knowledge in clinical pharmacology. However, our belief is that these areas cannot be defined by degree or educational background, but rather by the interest and training of the individual scientist/practitioner. For example, individuals with M.D., Pharm.D., D.O., or D.D.S. degrees may all be directly involved in patient care in a formalized healthcare setting. Thus, clinical pharmacology is delivered in this setting by individuals with differing doctoral backgrounds, yet these individuals share specific training related to their therapeutic areas of expertise. Other clinical pharmacologists are involved primarily in developmental research related to new therapeutic entities. These individuals often practice in an academic, industrial or government setting, and may not be involved in direct patient care. Nonetheless, their contribution to optimal therapeutic response is just as vital as that of practitioners who are directly involved in the evaluation of drugs in a clinical setting. In a similar vein, individuals with differing degrees and backgrounds participate in this specific research area, and many with professional practice doctorates do not see patients, but rather are involved in clinical pharmacology in the strictest sense of a research practice. Thus, regardless of degree or area of contribution, all individuals who are involved in research that contributes to improved therapeutic care for patients are clinical pharmacologists.

Consistent with the development of the discipline, and essential for its representation to the public, there is a need for a formal organizational structure to share and exchange knowledge related to the discipline. The College believes that it is essential for all individuals participating in the field to have an opportunity to share the results of their studies, participate actively in forums for the exchange of new information related to therapeutics, and have a voice in the development of policies, procedures and principles related to the discipline. To this end, the

College also believes that there should be an organizational structure in which all individuals have the opportunity to select the governing structure for said organization and the opportunity to play an active role in the conduct of activities by an organization representing the discipline.

The principles articulated in this document have been defined and ratified by the Board of the Regents of the American College of Clinical Pharmacology in an effort to promote harmony within the discipline. These principles provide a background for the definition of a clinical pharmacologist, and delineation of responsibilities associated with the discipline. Hopefully, this document will provide a stimulus for further discussion and growth of clinical pharmacology as we move into the next millennium.