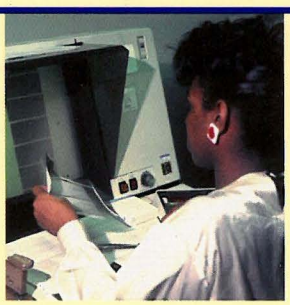
Pharmaceutical Research and

Manufacturers of America Foundation

1994 Annual Report

Dedicated to

The Foundation's



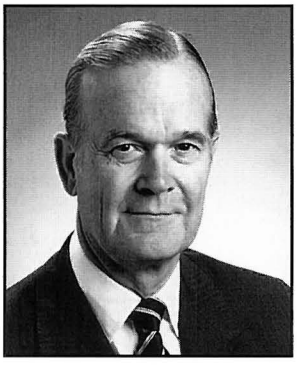
Benefactors

DEDICATED TO THE FOUNDATION'S BENEFACTORS

ABBOTT LABORATORIES FUND ● ALLERGAN, INC. ● ALZA CORPORATION ● AMERICAN HOME PRODUCTS CORPORATION ● ANAQUEST, INC. ● ASTRA USA, INC. ● B. F. ASCHER & COMPANY, INC. ● BERLEX LABORATORIES ● BOEHRINGER INGELHEIM CORPORATION ● BOOTS PHARMACEUTICALS, INC. ● BRISTOL-MYERS SQUIBB FOUNDATION ● BURROUGHS WELLCOME CO. ● CARTER-WALLACE, INC. ● CIBA-GEIGY CORPORATION ● CONNAUGHT LABORATORIES, INC. ● DUPONT MERCK PHARMACEUTICAL COMPANY ● ELI LILLY AND COMPANY FOUNDATION ● FISONS CORPORATION ● GENENTECH, INC. ● GLAXO INC. ● HOECHST-ROUSSEL PHARMACEUTICALS INC. ● HOFFMANN-LA ROCHE INC. ● JOHNSON & JOHNSON ● KNOLL PHARMACEUTICAL COMPANY ● LEDERLE LABORATORIES ● MARION MERRELL DOW INC. ● THE MERCK COMPANY FOUNDATION ● MILES FOUNDATION ● ORGANON INC. ● PFIZER INC. ● THE PROCTER & GAMBLE COMPANY ● REED & CARNICK ● RHONE-POULENC RORER ● SANDOZ PHARMACEUTICALS CORPORATION ● SCHERING-PLOUGH FOUNDATION, INC. ● SEARLE ● SMITHKLINE BEECHAM FOUNDATION ● SOLVAY PHARMACEUTICALS ● STERLING WINTHROP INC. ● SYNTEX CORPORATION ● 3M PHARMACEUTICALS ● THE UPJOHN COMPANY ● WARNER-LAMBERT FOUNDATION ● ZENECA PHARMACEUTICALS GROUP

CONTENTS

REPORT OF THE CHAIRMAN



Charles A. Sanders, M.D.
Chairman, Pharmaceutical Research and Manufacturers of America Foundation

The mission remains constant; only the name has changed. For twenty-eight years, the PhRMA Foundation functioned to provide support to young biomedical scientists and researchers. During the May 1994 meeting of the Foundation Board of Directors, official action was taken to change the name of the Foundation to the Pharmaceutical Research and Manufacturers of American Foundation.

There are several reasons for this name change, most significantly to reinforce and focus the Foundation's mission of support for research in the biomedical sciences. Since the Pharmaceutical Manufacturers Association membership had previously changed its name to Pharmaceutical Research and Manufacturers of America (PhRMA) and since the Foundation receives its support from PhRMA members, it seemed appropriate to make a similar change in the Foundation's name. Although PhRMA and the PhRMA Foundation are separate corporate entities, we felt a parallel change would help avoid confusion.

The research intensive pharmaceutical industry, most recently under the pressure of multi-dimensional healthcare reform efforts, has undergone tremendous change from corporate mergers to intense competitive pressures, from emphasis on production efficiencies to refined focus on selected research objectives, from new alliances to joint marketing ventures. The new name more accurately reflects the emphasis that the research-intensive pharmaceutical industry has placed on research for new chemicals and products. It says, more precisely, what the industry does.

The PhRMA Foundation currently sponsors twelve educational and training programs in the fields of basic and clinical pharmacology, toxicology, pharmaceutics, and a new program discipline—pharmacoeconomics—which we are proud to announce.

The very first program undertaken by the Foundation, shortly after its inception in 1965, was a Faculty Awards program in Clinical Pharmacology. The Foundation's Board, at that time, had come to the conclusion that clinical pharmacology had a bright future, and that it could best be stimulated through assisting, through financial support, bright young faculty members in the field. Such support has enabled a substantial number of such researchers and faculty members to get a solid and credible start in a much-needed scientific discipline.

And so it is in 1994 with pharmacoeconomics. The PhRMA Foundation Board has authorized initiation of a pilot program in Faculty Awards in Pharmacoeconomics in an effort to catalyze sufficient interest in the rapidly growing field of pharmacoeconomics. The new discipline is evolving as an evaluative science which examines cost effectiveness, cost benefits and research outcomes—comparing the value of pharmaceuticals and the value of the quality of life with costs. Beginning in 1995, the Foundation will fund two such awards. This is a modest start for such a needed program but, given the realities of current industry economics, we feel it is a nearly heroic commitment at a time when other programs are being reduced. I am proud to add this program to the Foundation's recent accomplishments.

This is my third year reporting to the Foundation's constituents as Chairman of the Board and my pride in the organization continues to grow. Reelected and continuing to serve with me during 1994-1995 are: Philip R. Tracy, PhRMA Foundation Vice Chairman and President and Chief Executive Officer of Burroughs Wellcome Co., Robert C. Black, PhRMA Foundation Treasurer and President of Zeneca Pharmaceuticals, and Maurice Q. Bectel, PhRMA Foundation President.

In addition, the following are serving on the PhRMA Foundation Board of Directors: Gordon M. Binder, Chairman and Chief Executive Office of Amgen, G. Gilbert Cloyd, Vice President, Pharmaceuticals, Procter & Gamble USA, Jan Leschly, Chief Executive of SmithKline Beecham, Herbert Sosman, President of Wallace Laboratories, Carter-Wallace Inc., Sidney A. Taurel, Executive Vice President and President, Pharmaceutical Division, Eli Lilly and Company, Robert N. Wilson, Vice Chairman, Board of Directors, Johnson & Johnson, Patrick J. Zenner, President and Chief Executive Officer, Hoffmann-La Roche Inc., Gerald J. Mossinghoff, President of Pharmaceutical Research and Manufacturers of America, (*Ex-Officio*).

My appreciation is extended to the PhRMA Foundation's current and former officers and Board members, to those firms whose support make the success of the Foundation possible, to the scientists who advise the Foundation on its programs, and to Foundation President Maurice Q. Bectel and his staff, whose efforts make it happen.

Charles A. Sanders, M.D.
Chairman, PhRMA Foundation
Chairman
Glaxo Inc.

REPORT OF THE PRESIDENT

Maurice Q. Bectel, D.Sc.
President, Pharmaceutical Research and Manufacturers of America Foundation

In the recent issue of the Foundation's publication *Scholars*, we editorially dedicated the issue to the Foundation's benefactors—those research-intensive pharmaceutical firms who have funded the Foundation's programs since its inception. In the aggregate, this relatively small number of companies has contributed more than $36 million, through the Foundation, in support of young biomedical scientists and researchers.

But the current economy and climate in which our industry finds itself does not provide the opportunity to expand programs the way we would like—or even feel that we have an obligation to support. As Chairman Sanders points out, the industry is struggling with a variety of pressures, mergers, healthcare reform, alliances, and other influences which are having a profound effect on the companies' bottom line—which eventually must have an effect on their contributions to the Foundation.

As a result, my report to the Foundation's Board of Directors addressed some operational changes that we are implementing, without doing irreparable structural damage to the Foundation despite a revenue reduction. As an example, nearly all of the Foundation's programs have been downsized. Although the Foundation Board of Directors authorized the development of a program in pharmacoeconomics to start in 1995, the action was balanced by the elimination of another program which, it was felt, had accomplished its objective over the years. This current direction is not of our choosing but is dictated by current fiscal reality.

Nonetheless, the PhRMA Foundation continues on its mission and can point to many individual and collective positive accomplishments in its 28-year history. Does anyone believe that the future demand and need for capable, dedicated young scientists and researchers in the biomedical sciences will diminish? And, if the need continues, the Foundation must do all in its power to maximize the resources at hand.

As the research-intensive pharmaceutical industry regains stability following this period of upheaval, we are confident that their support to the PhRMA Foundation will, once again, be on the increase. With that renewed support, the Foundation will be positioned to once again fund a larger percentage of the qualified applications in the twelve program areas we have identified as most in need of Foundation support—and perhaps, even, to fund newly identified areas of need for the Foundation's support.

Such flexibility and continuing commitment to supporting the development of young scientists and researchers for America's future health needs is what makes the PhRMA Foundation one of the pharmaceutical industry's centerpieces.

Maurice Q. Bectel, D.Sc.
President

MEETINGS AND OTHER ACTIVITIES

Twenty-Third Annual Awardee Meeting

The PhRMA Foundation Annual Awardee Meeting was held this year on January 19-20 at the Washington Vista International Hotel, in Washington, D.C. In spite of the accumulating snow, over 100 current and former awardees, as well as committee members from academe and industry, and PhRMA Foundation staff attended. They were honored to hear Gertrude B. Elion, D.Sc., Scientist Emeritus of The Wellcome Research Laboratories, Burroughs Welcome Co., speak on "The Lure of Pharmaceutical Research." Dr. Elion, who won the Nobel Prize for Physiology/Medicine in 1988, delivered the Thomas E. Hanrahan Memorial Speech. All those attending the PhRMA Foundation Annual Meeting welcomed Dr. Elion, and found her presentation both exciting and informative.

Preceding Dr. Elion's lecture was the Poster Session where current and former awardees displayed their research. This event plays a meaningful role in the Annual Meeting in that it provides those participating an opportunity to discuss with other awardees and committee members their theories and findings and to exchange ideas—a necessity for the advancement of biomedical research. As is customary, the three afternoon subgroup sessions in clinical pharmacology, basic pharmacology and pharmacology-morphology allowed attendees to hear presentations regarding their specific disciplines.

Charles A. Sanders, M.D., Chairman of the PhRMA Foundation Board, and Chairman of Glaxo Inc., delivers welcoming remarks to awardees, advisory committee members, staff and other Board members at the Annual Awardee Banquet, January 19, 1994.

Gertrude B. Elion, D.Sc., Nobel Prize Winner and Scientist Emeritus for the Wellcome Research Laboratories of Burroughs Wellcome Co., delivers the Thomas E. Hanrahan Memorial Lecture, January 20, 1994, Washington, D.C. In spite of a snow storm which closed the city, over 100 current and former awardees attended the session to hear Dr. Elion.

The Annual Awardee banquet was held on the evening of January 19 providing everyone with an opportunity to interact with PhRMA Foundation Board members and Advisory Committee members. The evening's events included an after-dinner presentation by PhRMA Foundation Board Chairman Charles Sanders, Chairman of Glaxo Inc.

PhRMA Foundation Board of Directors Spring Meeting, Washington, D.C.

At its May 2, 1994, meeting, this year held in Washington, D.C., the PMA Foundation Board of Directors elected to change the name of the Foundation to "The Pharmaceutical Research and Manufacturers of America Foundation." The Association had decided to change its name to more accurately reflect the emphasis that the research-intensive pharmaceutical industry has placed on research. Since the Foundation receives its support from PhRMA members, the PMA Foundation Board felt it was appropriate to also change the name of the Foundation.

Also, at its meeting, the Board re-elected as its Chairman Charles A. Sanders, M.D., Chairman of Glaxo Inc. Mr. Philip R. Tracy, President and Chief Executive Officer of Burroughs Wellcome Co., was re-elected Vice Chairman; and Mr. Robert C. Black, President of Zeneca Pharmaceuticals, was re-elected Secretary-Treasurer. The PhRMA Foundation Board welcomed two new members—Mr. Gordon M. Binder, Chairman and Chief Executive Officer of Amgen and Mr. Patrick J. Zenner, President and Chief Executive Officer, Hoffmann-La Roche Inc.

Ten pharmaceutical company executives serve on the current Foundation Board of Directors along with Gerald J. Mossinghoff, President of PhRMA, who is an *ex-officio* member. In addition to Sanders, Tracy, Black and new Board members Binder and Zenner, Board members serving are: Mr. G. Gilbert Cloyd, Vice President, Pharmaceuticals, Procter & Gamble USA; Mr. Jan Leschly, Chief Executive, SmithKline Beecham; Mr. Herbert Sosman, President, Wallace Laboratories, Carter-Wallace, Inc.; Mr. Sidney A. Taurel, Executive Vice President and President, Pharmaceutical Division, Eli Lilly and Company; and Mr. Robert N. Wilson, Vice Chairman, Board of Directors, Johnson & Johnson.

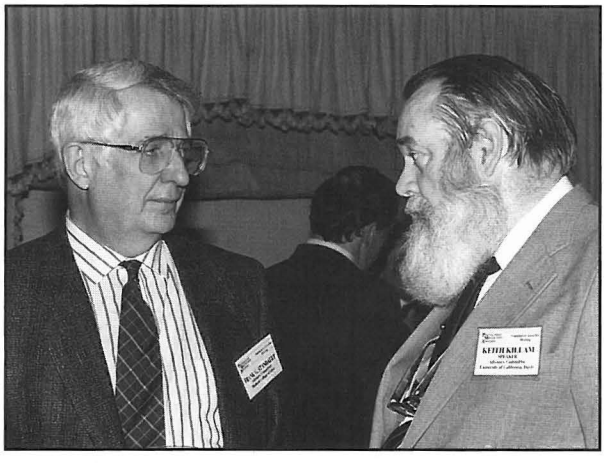
Pharmacoeconomics—A New Faculty Development Program in 1995

The PhRMA Foundation Board has boldly stepped out to authorize a pilot program in support of Pharmacoeconomics—an evaluative science which compares the quality of life provided by pharmaceuticals with costs. In 1995, the Foundation will support two Pharmacoeconomics Faculty members at schools of medicine, pharmacy, public health and economics for a two-year period. President Bectel applauds the Board for "stepping out in the face of uncertain horizons to address a definite need in the area of pharmacoeconomics."

Keith Killam, Jr., Ph.D., Speaks at PhRMA Foundation's Program During FASEB's Experimental Biology '94 Meeting

On April 24, the PhRMA Foundation was pleased to sponsor a scientific program through the American Society for Pharmacology and Experimental Therapeutics during FASEB's "Experimental Biology '94" Meeting in Anaheim, California. Longtime friend and Advisory Committee member Keith F. Killam, Jr., Ph.D., was our distinguished speaker and delivered a fascinating presentation on "The New Face of Pharmacology." The session attracted over 60 of Keith's colleagues—former and current awardees, pharmacology department chairmen, other advisory committee members, as well as ASPET officials. Also attending were Keith's lovely wife, Eva and daughter, Anne. Dr. Killam is Professor and Former Chairman of the Department of Medical Pharmacology at the University of California, Davis, School of Medicine and has served on the Foundation's Basic Pharmacology Advisory Committee for over 21 years.

In 1994, FASEB members jointly met in April with Experimental Biology '94 and the PhRMA Foundation was very pleased to participate through ASPET. In the past, the Foundation program was held in the fall in conjunction with ASPET's annual meeting. This year marked the first scientific program for the Foundation under this new format.



After his well received presentation at the PhRMA Foundation program during the ASPET/FASEB meeting, Keith Killam, Jr., Ph.D., recaps a few points with colleague Frank Standaert, M.D., who also serves on the Basic Pharmacology Advisory Committee.

EDUCATION AND TRAINING PROGRAMS

The PhRMA Foundation's primary mission is to promote the betterment of public health through scientific and medical research by providing funding to university-based scientists, researchers and educators. Foundation goals in education and research are accomplished through its twelve funding programs —four in clinical pharmacology, two in pharmacology/toxicology, one in the combined field of pharmacology-morphology, three in pharmaceutics, and one in pharmacoeconomics (new in 1995). The Research Starter Grant provides starter funds in pharmacology, clinical pharmacology, drug toxicology and pharmaceutics. The Foundation also accepts applications in all program areas for research on drugs for rare diseases.

CLINICAL PHARMACOLOGY

The clinical pharmacology program provides funding for four levels—students, postdocs, faculty and directors of new clinical pharmacology units.

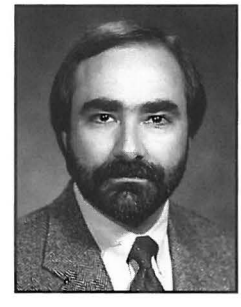
Faculty Awards in Clinical Pharmacology

Through the Faculty Development Awards in Clinical Pharmacology program, the Foundation makes three-year awards to medical schools for salary and fringe benefits support of full-time junior faculty members.

The Foundation has set a ceiling of $40,000 on the amount of its participation in total yearly salary and fringe benefits for any candidate.

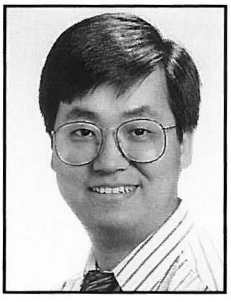
With the awards beginning July 1, 1994, 101 individuals have been supported under this program since 1967.

Recipients of the awards which began July 1994 are:

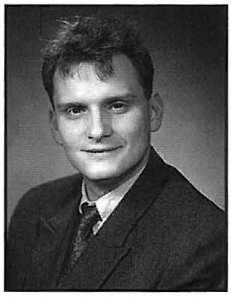


Richard D. Huhn, M.D., Assistant Professor, Clinical Pharmacology Program, Robert Wood Johnson Medical Center, University of Medicine and Dentistry of New Jersey and The Cancer Institute of New Jersey: Clinical Pharmacology of Hematopoietic Cytokines." The awardee's academic plan will have three components: (1) A program in clinical pharmacology of hematopoietic cytokines. A clinical trial of sequentially combined recombinant human interleukin-3 and granulocyte colony-stimulating factor to optimize the recruitment of circulating hematopoietic progenitor cells for transplantation will be conducted on the basis of pharmacokinetic/pharmaco-

dynamic data developed in a prior trial conducted by the candidate. This trial will provide pharmacodynamic information from which to plan larger efficacy trials of hematopoietic support following dose-intensive chemotherapy; (2) An extramural research training activity focusing on the effects of basic fibroblast growth factor on the expression of the GM-CSF receptor and adhesion of progenitors to marrow stromal extracellular matrix. This project will provide the awardee with experience in advanced molecular techniques in an institution devoted to hematopoiesis research; (3) Academic activities of the Program in Clinical Pharmacology will be developed to provide educational and clinical services to the Medical School.



Richard B. Kim, M.D., Assistant Professor, Division of Clinical Pharmacology, Vanderbilty University School of Medicine: "Characterization of Hepatic Carrier-Mediated Processes Involved in the Uptake and Biliary Excretion of Oligopeptides and Identification of the Individual Protein Transporters by Cloning Approaches." The proposed studies are designed to improve the understanding of the carrier-mediated processes involved in uptake and biliary excretion of oligopeptides in the liver. Compounds known to be avidly taken up in an energy-dependent fashion by the liver and predominantly excreted intact in bile will be used to characterize such transport and its driving force(s) by basolateral and canalicular membrane vesicles. Subsequently, PCR-based homology screening and recombinant vaccinia virus-based transient expression systems will be utilized to obtain the specific cDNA clone(s) encoding oligopeptide transporter function. This will then allow structure-function studies of the protein(s) expressed by the cloned cDNA(s). Availability of such information will ultimately lead to a better understanding of the determinants of hepatic transport, and will permit a more rational design of oligopeptides as therapeutic agents.



Andre Terzic, M.D., Instructor in Medicine and Pharmacology, Mayo Clinic, Mayo Medical School (Mayo Foundation): "Molecular Pharmacology of Cardiotonic and Cardioprotective Regulation." Cardiac failure and ischemic heart disease are major causes of mortality, prompting the search for new means of pharmacotherapy. Dr. Terzic has discovered that myocardial á 1-adrenoceptors increase force and intracellular pH (pH_i) by activating the Na/H antiport. Since the pharmacological modulation of pH_i has not yet been exploited to develop cardiotonic agents, the first aims of this proposal is to investigate the á 1-adrenoceptor-mediated pH-dependent regulation of contractility. For ischemic preconditioning, a cardioprotective mechanism in which brief ischemia episodes render the myocardium resistant to subsequent more sustained ischemia, ATP-sensitive K^+ (KATP) channels appear to be essential. Understanding how KATP channels open should prove useful to pharmacologically induce preconditioning. Thus, the second aim of this proposal is to study the mechanism(s) of KATP channel activation by potassium channel openers and GTP-binding proteins, which

I have found to activate KATP channels. Patch clamp electrophysiology and microspectrofluorometry will be employed to address these aims. The significance of this program is to gain insight into the molecular modulation of pH_i and KATP channels, as a basis to design new cardiotonic and cardioprotective agents.

Recipients of the award which began July 1993 are:

Evan D. Kharasch, M.D., Ph.D., Assistant Professor, Department of Anesthesiology, University of Washington, School of Medicine.

David W. Rudy, M.D., Assistant Professor, Department of Medicine, Indiana University, School of Medicine.

Jason Gari Umans, M.D., Ph.D., Assistant Professor, University of Chicago, Pritzer School of Medicine.

Those who entered the second year of their award in 1993 are:

Joshua Olajide Atiba, M.B., Assistant Professor of Medicine and Pharmacology, University of California, Irvine (actually began his second year in 1994).

Margaret Ann Smith Dordal, M.D., Ph.D., Assistant Professor of Medicine, Northwestern University Medical School.

Leslie A. Lenert, M.D., Assistant Professor, Department of Medicine, Stanford University.

Raymond J. Hohl, M.D., Assistant Professor, Department of Internal Medicine, University of Iowa.

Individuals who entered the third year of their award in 1993 are:

Michael J. Jamieson, M.B.Ch.B., M.R.C.P., Assistant Professor, University of Texas Health Science Center.

Theresa A. Shapiro, M.D., Ph.D., Assistant Professor of Medicine, Johns Hopkins University School of Medicine.

Those individuals who ended their awards in 1993 are:

Joseph J. Crowley, M.D., Assistant Professor, Division of Geriatric Medicine, University of Washington.

Paolo B. DePetrillo, M.D., Instructor, Department of Medicine, Brown University.

Charles W. Flexner, M.D., Assistant Professor, Department of Medicine and Department of Pharmacology, The Johns Hopkins University School of Medicine.

Joseph F. Foss, M.D., Assistant Professor, Department of Anesthesia and Critical Care, Committee on Clinical Pharmacology, University of Chicago.

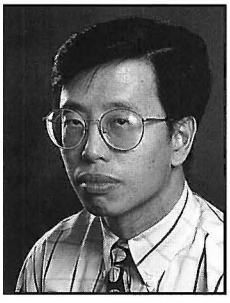
Fellowships for Careers in Clinical Pharmacology

The second program in clinical pharmacology provides "Fellowships for Careers in Clinical Pharmacology." This award offers clinicians an opportunity for intensive study in any of the basic sciences that fall within the general field of pharmacology. The program is open to physicians, dentists, and veterinarians who are well into their clinical training and wish to pursue careers in clinical pharmacology. With the year or two of support offered by this fellowship program, depending on the particulars of the undertaking, the individual can pursue full-time study in the basic pharmacologic sciences needed to complement his clinical skills.

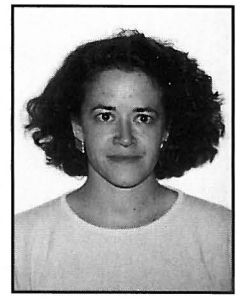
The program allows an individual to apply for a fellowship two years in advance of the activation date of the award. For example, those applying for a fellowship in the fall of 1994 may request that the fellowship begin July 1995 or July 1996.

First awards under this program were made in 1973. Since that time, 59 fellowships have been awarded.

Recipients of the awards beginning July 1, 1994:

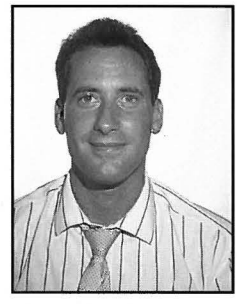


Richard Z. Lin, M.D., M.P.H., Stanford University School of Medicine: "A Mechanism of α-Adrenergic Receptor Desensitization; Endothelium-Derived Relaxing Factor." Regulation of smooth muscle tone and peripheral resistance by catecholamines is important in the maintenance of normal blood pressure. The responsiveness of blood vessels to catecholamines may be modified in a variety of settings including hypertension and altered hormonal states. Additionally, catecholamines may themselves regulate the sensitivity of a vessel to subsequent stimulation by sympathomimetic drugs. Desensitization is a process by which after a cell or tissue has been exposed for a period of time to an agonist hormone or drug such as a catecholamine, the tissue often becomes less responsive to further stimulation by that agent. The manifestations of desensitization of drug responses have clinical implications as well as insight into cellular adaptive and regulatory mechanisms. Dr. Lin's research involves the investigation of mechanisms by which catecholamines induce desensitization of á adrenergic receptor-mediated responses in smooth muscle. One such mechanism involves the vascular endothelium releasing an enhanced amount of endothelium-derived relaxing factor (EDRF). The major focus of this research is to investigate mechanisms underlying this adaptation. Specifically, to determine the á adrenergic receptor subtype transducing the signal to increase EDRF release; (2) determine if the mechanism for increased EDRF release involves increased expression of nitric oxide synthase; and (3) explore the pathophysiological significance of the enhanced release of EDRF in models of disease such as pheochromocytoma and prolonged infusion of vasopressors.



Merit Cudkowicz, M.D., Harvard Medical School, Harvard University: "Therapeutic Trial of Free Radical Scavengers in Amyotrophic Lateral Sclerosis." This study will test the hypothesis that free radical toxicity causes Amyotrophic Lateral Sclerosis (ALS). In several families with ALS, the disease is co-inherited with mutations, in the gene for copper/zinc superoxide dismutase (SOD1), an enzyme which detoxifies the free radical superoxide. These mutations decrease the activity of SOD1. The clinical and pathological similarities between familial and sporadic ALS imply that sporadic ALS may also be a consequence of free radical toxicity.

The study will involve both familial ALS and sporadic ALS patients and will consist of (1) a placebo controlled trial of multiple oral antioxidants, and (2) a trial of intrathecal delivery of SOD1. The drug delivery system for administration of SOD1 and the pharmacokinetics of SOD1 will be analyzed. Drug efficacy will be gauged both by clinical outcome and by analysis of laboratory parameters which we believe reflect disease activity.



Raymond W. Urbanski, M.D., Ph.D., Jefferson Medical College, Thomas Jefferson University: "Targeted Cytotoxicity of Colorectal Tumors by E. Coli ST." Colorectal cancer is a leading cause of cancer and cancer-related death in the U.S. A significant impact on this disease could be achieved by developing agents which specifically detect and treat local and metastatic disease. One approach to the diagnosis and therapy of malignancies is the utilization of molecules targeted to determinants expressed selectively by tumors. These studies will define the kinetic characteristics of ST-receptor internalization in human colon carcinoma cells *in vitro*. Intracellular processing of endocytosed ST will be examined by anlayzing radioactive metabolites of ST recovered intracellularly and in the *metoconfocal* microscopy. Once internalization and processing have been characterized, cytotoxins appropriate to the intracellular compartment targeted by ST will be chemically conjugated to ST to define coupling strategies yielding conjugates with preservation parameters of this cytotoxicity will be defined. These studies will be extended to different human colon carcinoma cell lines established *in vitro*, to asses the potential for heterogeneity of the responsiveness of tumors. Finally, the cytotoxicity of these conjugates in cells obtained directly from colorectal tumors of patients will be defined. These studies will establish the utility of ST as a specific targeting agent to deliver diagnostics and therapeutics to primary and metastic colorectal tumors and will form the basis for studies of their efficacy in *in vivo* animal models in the future.

Beginning his award in July of 1993:

Merlin R. Hamre, M.D., M.P.H., Northwestern University Medical School.

Entering the second year of his award in 1993:

Gene R. Pesola, M.D., Postdoctoral Fellow, Department of Pharmacology, Medical University of South Carolina.

Individuals who ended their award in 1993 are:

Nabil S. Andrawis, M.D., Ph.D., Program in Clinical Pharmacology, Department of Medicine, Brown University School of Medicine.

Andre Terzic, M.D., Ph.D., Mayo Clinic, Mayo Foundation.

Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology

The Foundation's third program is the Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology. This program, which began in 1974, offers students an opportunity to spend up to two years full-time conducting an investigative project in pharmacology-clinical pharmacology. The minimum period of the award is three months and maximum is two years. It is hoped that by having students become involved in investigative projects at a point when career choices are still relatively flexible, they will eventually choose research careers in clinical pharmacology. One-hundred twenty-one awards have been made since 1974.

Individuals whose awards began in July 1994 are:

Anne Jeannette Blaschke, University of California, San Diego, School of Medicine (one year)—"Identifying New Helix-Loop-Helix Genes from Novel CNS Cell Lines". Ms. Blaschke's fellowship supervisor is Jerold Chun, M.D., Ph.D., Assistant Professor of Pharmacology.

David Dybdal, Georgetown University School of Medicine (two years)—"Subthalamic Control of GABAergic Output from the Substantia Nigra." Mr. Dybdal's principal advisor is Karen Gale, Ph.D., Professor of Pharmacology.

Hoa Le, University of California, Irvine, College of Medidine (three months)—"Characterization by Quantitative Autoradiography for NPY Receptor Subtypes in Rat Mesentery." Mr. Le's principal advisor is Sue P. Duckles, Ph.D., Professor of Pharmacology.

Susan E. Sparks, The Finch University Health Sciences, Chicago Medical School (one year)—"Pharmacological Manipulation of β-Globin Genes." Ms. Sparks's fellowship supervisor is Donna King, Ph.D., Assistant Professor of Pharmacology and Molecular Biology.

Robert A. Stoltz, New York Medical College (one year)—"Cellular and Molecular Signalling of 12(R) - HETrE in Microvessel Endothelial Cells." Mr. Stoltz's principal supervisor is Michael L. Schwartzman, Ph.D, Professor of Pharmacology.

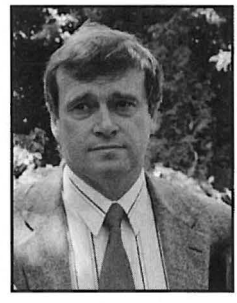
Raymond P. Ward, University of Washington, School of Medicine (one year)—"Localization and Regulation of the 5HT-6 Receptor in Rat Brain—Characterization of the Rat Serotonin 5-HT6 Receptor." Mr. Ward's principal advisor is Daniel Dorsa, Ph.D., Professor and Director of Neuroscience Research, Department of Pharmacology/Psychiatry.

Nader Yaghoubi, Boston University, School of Medicine (one year)—"Electrophysiological Investigation of the Role of Phosphorylation in Regulation of $GABA_a$ Receptors expressed in Xenopus Oocytes." Mr. Yaghoubi's fellowship supervisor is David H. Farb, Ph.D., Chairman of the Department of Pharmacology and Experimental Therapeutics.

Clinical Pharmacology Unit Support

This program assists directors of clinical pharmacology units established within a two-year period preceding the award, or units that have acquired a new director during that period. The purpose of the program is to provide supplementary funds to assist the unit's research efforts until other research grants are obtained. The first grants were made in 1978 and the total number of awards made to date is twenty-five. The Foundation, with the support of the Clinical Pharmacology Advisory Committee, the Scientific Advisory Committee and the Board of Directors, has decided to temporarily suspend this program for 1995.

Beginning his award in July of 1994:



George H. Lambert, M.D., Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey. The Division of Pediatric Pharmacology and Toxicology of the Department of Pediatrics at the Robert Wood Johnson Medical School was established in the fall of 1993. The main focus of the Division will be to examine and understand the expression and regulation of drug metabolizing enzymes throughout human development, and also the effects of pregnancy and lactation on the maternal expression and regulation of drug metabolizing enzymes. The drug metabolizing enzymes of study will be the cytochrome P450 super gene family of enzymes. The constitutive expression and regulation, and the effects of disease states, drugs, environmental chemicals and diet on their expression and regulation will be examined. The laboratory is being equipped to address the questions using molecular and biochemical techniques and stable isotopes. The stable isotopes will be used to label substrates that are biomarkers of the cytochrome P450 enzymes. The safety and sensitivity of these isotopically labeled biomarkers are of particular importance when the studies involve children.

BASIC PHARMACOLOGY

Faculty Development Awards in Basic Pharmacology

The Faculty Development Award in Pharmacology was initiated to strengthen basic pharmacology by helping to maintain existing academic capability and, ultimately, to expand the field by enlarging the faculty base. To meet this goal, support is provided to full-time junior faculty members who give promise of outstanding accomplishments.

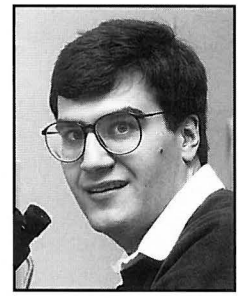
The first awards were made in 1973 and are for a two-year period. The program provides salary and fringe benefits. The Foundation has set a ceiling of $30,000 on the amount of its participation in the total yearly salary and fringe benefits for awardees. The total number of awards made to date is 62.

Recipients of the 1994 Faculty Development Awards in Pharmacology are:

James E. Ferrell, Jr., M.D., Ph.D., Stanford University, School of Medicine—"The Link from Ras to Raf-1." Ras proteins play a key role in cell growth control and cell fate determination, and may play a role in the function of terminally differentiated cells as well. Recent work has provided a detailed understanding of how Ras receives signals from diverse cell surface receptors. Activated Ras can activate a protein kinase cascade that includes Raf-1 and MAP kinase. Ras can interact physically with Raf-1, the most upstream member of the cascade, but activation of Raf-1 by Ras requires at least one additional factor that has yet to be identified. The unidentified linking factor is arguably the most important gap in our understanding of Ras signaling. Here Dr. Ferrell proposes to purify the linking factor from an unusually good source, *Xenopus* oocyte cytoplasm, and then clone, sequence, and characterize it. He hopes to gain insight into the molecular basis of cell growth control, and to identify a new target for screening of potential therapeutic agents.

Ming Li, Ph.D., University of South Alabama, College of Medicine, "Functional Regulation of Sodium Channels by Voltage-Dependent Phosphorylation with cAMP-Dependent Protein Kinase in the Mammalian Neuron." The whole cell and single channel patch clamp recording techniques will be used to investigate the regulation of sodium channels by cAMP-dependent protein kinase in a voltage-dependent manner. The voltage-dependent phosphorylation may have two major effects on sodium channel function: (1) modulation of transient voltage-dependent potentiation which would affect the threshold for the generation of the action potential, and (2) removal of use-dependent slow inactivation which would regulate the firing frequency in central neurons. In combination, these parameters regulate information processing by neurons. The sodium channel activation and slow inactivation will be characterized under the conditions that optimize voltage-dependent phosphorylation catalyzed by cAMP-depen-

dent protein kinase. The function of dephosphorylation in voltage-dependent phosphorylation by endogenous and exogenous phosphatases will also be investigated. These studies will be conducted with primary cultured embryonic rat brain nervous cells.



Brian E. Wadzinski, Ph.D., Vanderbilt University, School of Medicine—"Localization and Targeting of Protein Ser/Thr Phosphatases in Mammalian Cells." Protein serine/threonine phosphatases (PPs), especially nuclear PPs, play an integral role in the control of cell growth and differentiation. One of Dr. Wadzinski's overall goals is to focus on the purification and characterization of these nuclear phosphatases, in particular PP2A and PPX, which at the present time has not been done. To accomplish this goal, Dr. Wadzinski must first determine PP expression and localization in mammalian cells. The primary goals of the study is to obtain data concerning the subcellular distribution of these phosphatases and, in particular, identification of the phosphatases which are nuclear-localized or redistributed to the nucleus in response to hormone/growth factor. Dr. Wadzinski will examine the tissue distribution and subcellular localization of these enzymes by utilizing the following complementary techniques; *in situ* hybridization, immunoblotting of tissues and subcellular fractions, and immunocytochemistry. The availability, in Dr. Wadzinski's laboratory, of full-length phosphatase cDNAs and specific anti-peptide antibodies makes these studies feasible. These results will provide the groundwork in identifying the enzymes. Dr. Wadzinski will study at the molecular level to define the precise phosphorylation/dephosphorylation events underlying cell cycle and transcriptional regulation.

Individuals who began their awards in July of 1993:

Mark Leid, Ph.D., Assistant Professor, Oregon State University, College of Pharmacy.

Elias Lolis, Ph.D., Assistant Professor, Department of Pharmacology, Yale University, School of Medicine.

Bih-Hwa Shieh, Ph.D., Assistant Professor, Department of Pharmacology, Vanderbilt University, School of Medicine.

Entering their second year in 1993:

Todd A. Verdoorn, Ph.D., Assistant Professor, Department of Pharmacology, Vanderbilt University School of Medicine.

Roseann L. Vorce, Ph.D., Assistant Professor, Department of Pharmacology, University of Nebraska Medical Center.

William Frederick Wonderlin, Assistant Professor, Department of Pharmacology and Toxicology, West Virginia University, School of Medicine.

Those who concluded their awards in 1993 are:

Stewart N. Abramson, Ph.D., Assistant Professor, University of Pittsburgh, School of Medicine.

Rodney Kawahara, Ph.D., Assistant Professor, University of Nebraska Medical Center.

Scott A. Waldman, M.D., Ph.D., Assistant Professor, Thomas Jefferson University, Jefferson Medical College.

Fellowships for Advanced Predoctoral Training in Pharmacology or Toxicology

The PhRMA Foundation has developed the "Advanced Predoctoral Training in Pharmacologoy or Toxicology" program to increase the number of well-trained investigators in the field of pharmacological research in order for the discipline to thrive. This program is designed to encourage and support promising students during their thesis research and is aimed at those candidates who are within two years of completing their research for pharmacology/toxicology doctoral dissertations.

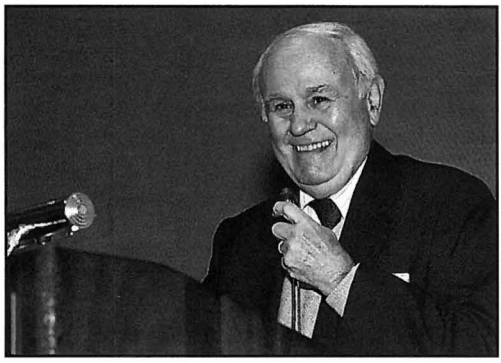
This fellowship program provides a stipend of $12,000 a year and $500 a year for incidentals directly associated with preparation of the dissertation. The program, in its 17th year, has awarded a total of 210 fellowships.

Those who have been awarded 1994 fellowships beginning between January through July are:

Colleen Marie Burns, Vanderbilt University, School of Medicine: "AMPA Receptor Subunit Expression in Experimental Models of Neurodegeneration"—Inappropriate calcium entry into neurons may play a role in neurodegeneration. Normally calcium impermeable AMPA-subtype glutamate receptors may contribute to neurotoxicity by converting to a calcium permeable form. Ms. Burns will address this hypothesis by examining AMPA receptors in experimental models of hypoxia-ischemia. *Thesis Advisor:* Ronald Emeson, Ph.D., Assistant Professor, Pharmacology.

Wayne O. Carter, Purdue University, School of Veterinary Medicine, "The Effect of Nitric Oxide and the Therapeutic Manipulation of this Recently Discovered Mediator in Endotoxemia"—Endotoxemia is a severe disease syndrome affecting both humans and animals. Nitric oxide is a recently discovered mediator in both physiologic and pathologic cellular mechanisms. This research will investigate the role of nitric oxide in endotoxemia with particular emphasis on neutrophil and endothelial cell interactions and function. *Thesis Advisor:* J. Paul Robinson, Ph.D., Professor and Director of Flow Cytometry Lab.

Patricia L. Cleveland-Wolfe, Cornell University, College of Veterinary Medicine, "The Pharmacological Dissection of the Calcium Influx Pathways of Mucosal Mast Cells"—The focus of this research is on the role of intracellular calcium handling in the regulation of mucosal mast cells, a cell type that has been shown to be important in several disease processes, such as human asthma and allergy. *Thesis Advisor:* Clare Fewtrell, Ph.D., Associate Professor of Pharmacology.



Robert B. Parks, Jr., M.D., Ph.D., Brown University E. E. Brintzenhoff Professor of Medical Science, introduces his longtime friend, Gertrude B. Elion, D.Sc. Dr. Elion was the PhRMA Foundation Annual Awardee Meeting guest speaker.

Shubhik Kumar DebBurman, Northwestern University, Medical School, "The Molecular Basis for Homologous Desensitization of the Human m2 Muscarinic Acetylcholine Receptor (hm2 mAChR)"—Muscarinic Acetylcholine Receptors are a family of neurotransmitter receptors. The role of protein phosphorylation in mediating the termination of hm2 mAChR-activated signalling will be investigated in this research. The G protein-coupled Receptor Kinases (GRKs) that phosphorylate the receptor *in vivo* will be identified and molecularly characterized. *Thesis Advisor:* Dr. M. Marlene Hosey, Professor of Pharmacology.

Joseph Erhardt, University of Pennsylvania, School of Medicine, "Identifying Genes Up-Regulated During Cell Death"—PC12 pheochromacytone cells can be differentiated into sympathetic-like cells that are dependent on nerve growth factor (NGF) for survival. When deprived of NGF, these terminally differentiated cells undergo an RNA and protein synthesis-dependent cell death. Using this system, these experiments represent an initial endeavor to identify biochemical and molecular events responsible for neuronal death following the loss of trophic support. *Thesis Advisor:* Randall N. Pittman, Ph.D., Associate Professor of Pharmacology.

Timothy D. Garver, Pennsylvania State University, College of Medicine, "Protein Phosphatases as Potential Therapeutic Targets in Alzheimer's Disease" —This project will attempt to elucidate the cascade of events involved in the phosphorylation/dephosphorylation of tau protein, a microtubule associated protein which is the major component of the neurofibrillary tangles of Alzheimer's Disease. The relative roles of protein kinases and phosphatases will be investigated while looking at possible points of therapeutic intervention. *Thesis Advisor:* Melvin L. Billingsley, Ph.D., Professor of Pharmacology.

Janice E. Kerr, Loyola University of Chicago, Stritch School of Medicine, "The Hippocampal Androgen Receptor: Regulation, Binding and Cellular Effects Following Long-Term Anabolic-Androgenic Steroid Treatment"—The increasing use of anabolic-androgenic steroids by athletes and reports of psychological side effects of these drugs has prompted a heightened research interest into the intracellular mechanisms of androgens in neural tissue. This research characterizes the rat hippocampal androgen receptor, its regulation and its effect on immediate early gene expression following high doses of anabolic steroids. *Thesis Advisor:* Dr. Sheryl G. Beck, Associate Professor of Pharmacology.

Lena Yuh-Pyng Lin, University of California, Los Angeles, School of Medicine, "3,4-Methylenedioxymethamphetamine (MDMA) Metabolism and the Possible Role of Cytochrome P45 in MDMA Toxicity"—The objective of this research is to determine the isozymes of cytochrome P450 that catalyze the metabolism of MDMA to two major electrochemically active metabolites, dihydroxymethamphetamine (DHMA) and an unidentified metabolite and to assess their involvement in the 5-HT selective neurotoxicity caused by MDMA. *Thesis Advisor:* Arthur K. Cho, Ph.D., Professor and Vice Chair of Pharmacology.

Matthew G. Melaragno, Michigan State University, College of Human Medicine, "Contribution of the Slow Pressor Effect of Angiotensin II to the Pathogenesis of Renovascular Hypertension"—The role of the hormone angiotensin II (AngII) is causing high blood pressure resulting from disease of the renal arteries is well established. However, the exact mechanism is not understood. This research is designed to test the hypothesis that renal artery disease results in increased responsiveness of blood pressure to AngII. *Thesis Advisor:* Gregory D. Fink, Ph.D., Professor of Pharmacology and Toxicology.

Shani C. Missner, Georgetown University, School of Medicine, "The Effect of Hormones and Cytotoxic Drugs on Heparin-binding Growth Factor Gene: Expression in Breast Cancer"—Breast cancer growth and metastasis requires the recruitment of new blood vessels. Previous research points out that the most potent endothelial cell growth factors released from breast cancer cells are heparin binding growth factors (HBGF's). The focus of this project is to study how conventional treatments affect HBGF gene expression in tumors. With this knowledge, the ultimate goal of this research is to design a new approach to breast cancer chemotherapy that combines conventional drugs with specific anti-HBGF targeted agents. *Thesis Advisor:* Anton Wellstein, M.D., Ph.D., Associate Professor of Pharmacology.

Heather K. Prince, Emory University, School of Medicine, "Changes in Glutamate AMPA Receptor Submit Composition in Amygdaloid Kindling" —Abundant evidence suggests that epilepsy may result from changes in excitatory neuro-transmission, the majority of which is mediated by the AMPA Glutamate receptor subtype. This project will study the role of the AMPA receptor in the development of epilepsy utilizing an animal model of epilepsy known as kindling. *Thesis Advisor:* P. Jeffrey Conn, Ph.D., Assistant Professor.

Ilsa I. Rovira, University of Missouri-Columbia, School of Medicine, "The Interactions Between the Insulin Receptor and the Insulin Receptor Substrate-1"—This study attempts to identify the specific sites required for the interaction between the insulin receptor and its substrate IRS-1, and the mechanism by which these two proteins interact and lead to insulin mediated cellular responses. *Thesis Advisor:* Dr. Peter A. Wilden, Assistant Professor of Pharmacology.

Zhengjin Tu, University of Minnesota, Medical School, Minneapolis, "Regulation of Salivary Gland-Specific Gene Expression by Isoproterenol and Dietary Tannins in Transgenic Mice"—Salivary glands and salivary gland proline-rich proteins (PRPs) play important roles in human oral health. This research will investigate the molecular mechanisms governing proline-rich proteins salivary specific and isoproterenol and dietary tannins regulatable gene expression using transgenic *in vivo* approaches. *Thesis Advisor:* Dr. David K. Ann, Assistant Professor of Pharmacology.

Bo Yunn Polly Ann Wong, Stanford University, School of Medicine, "The Cloning and Characterization of *Xenopus Laevis NimA*"—*NimA* is an essential regulator of cell division in a filamentous fungus. Ms. Wong has identified a related gene in a higher eukaryote, *Xenopus Laevis* and plans to test the hypothesis that NimA is a universal regulator of cell division. *Thesis Advisor:* James E. Ferrell, Jr., Assistant Professor of Molecular Pharmacology.

Hequn Yin, University of Rochester, School of Medicine, "Structure Activity Studies of HCFCs Metabolism and Toxicity"—Hydrochlorofluorocarbons (HCFCs) are being developed as replacements for the ozone-depleting Chlorofluorocarbons (CFCs). Current research is undertaken to study metabolism of HCFCs and tissue conjugation by their metabolic intermediates. Theoretical calculations will be combined to investigate the factors that govern the primary cytochrome P-450-catalyzed reaction rates. *Thesis Advisor:* M. W. Anders, D.V.M., Ph.D., Professor and Chairman of Pharmacology and Professor of Environmental Medicine.

Those who received fellowships in 1993 and continued in 1994 are:

Susan M. Cohen, Duke University, School of Medicine.

Henry M. Colecraft, University of Rochester, School of Medicine and Dentistry.

Bevin Page Engelward, Harvard School of Public Health (began award in 1994).

Guoping Feng, State University of New York at Buffalo, School of Medicine and Biomedical Sciences.

Michael S. Grotewiel, Vanderbilt University, School of Medicine.

Clarissa J. Haugsness, University of Kansas Medical Center, School of Medicine.

Saraswati R. Kenkare, University of California, San Francisco, School of Pharmacy.

Sheryl Ames Mason, University of South Carolina, School of Medicine.

James M. Rusnak, University of Pittsburgh, School of Medicine.

W. Bruce Sneddon, Dartmouth Medical School.

Elizabeth A. Thomas, University of California, Irvine, College of Medicine.

PHARMACOLOGY / MORPHOLOGY

Fellowship Awards in Pharmacology-Morphology

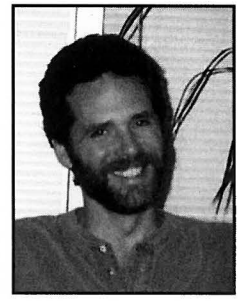
The purpose of this program is to increase our knowledge about the actions of drugs by direct study of their effects on cells and tissues; to correlate the morphological changes; and, concurrently, to uncover associations observed with functional parameters of cells and tissues.

The awards are two years each. The level of support varies and is aimed at keeping within the existing stipends for similarly trained individuals within the applicant university. First offered in 1968, 92 awards have been made to date.

In order to be eligible for an award, the candidate must possess formal training in a morphologic specialty or in pharmacology. However, subsequent training in the complementary discipline, during the period of the fellowship, may be informal. On completion of the program, the fellow should be able to use the tools and concepts of both disciplines.

Recipients of the fellowship beginning July 1994 are:

Min-Tsai Liu, D.D.S., Columbia University, College of Physicians and Surgeons, "Characteristics of Pancreatic Neurons and Their Response to 5-HT." Pancreatic ganglia are formed by precursor cells that migrate into the organ from the bowel (Kirchgessner et al., '92) and are innervated by neurons in the myenteric plexus of the stomach and duodenum (Kirchgessner and Gershon, '90). Enteric neurons are capable of activating neurons in the pancreatic ganglia, which in turn stimulate acini and islet cells. At present two types of enteropancreatic nerve have been identified. One is cholinergic, and it is possible to interrupt enteropancreatic signalling with nicotinic antagonists, such as hexamethonium. The other is serotonergic. In contrast to acetylcholine, 5-HT appears to be a modulator, affecting the degree of excitability of pancreatic neurons, rather than a transmitter. 5-HT receptors are present in pancreatic ganglia and are analogous to those found in the gut (Kirchgessner et al., '92; Kirchgessner et al. '93). Virtually nothing is known about the electrophysiological properties of pancreatic neurons, their response to 5'HT or enteric neural stimulation, and how they modulate exocrine and endocrine secretion. The immediate aim of the current research, therefore, is to analyze the electrophysiological properties of morphologically and chemically identified pancreatic neurons and the role of 5'HT in the enteropancreatic innervation.



Miles Orchinik, Ph.D., Rockefeller University, "Role of the $GABA_A$ System in Stress-induced Atrophy of Hippocampal CA3 Dendrites" (one year). The adult brain undergoes dynamic alterations in synaptic efficacy and neuronal morphology in response to experience or neuroendocrine environment. No where is this more evident that in the hippocampus, where learning and memory processes may be dependent upon such plasticity. Therefore, the discovery that repeated stress produces dendritic atrophy in the hippocampus may have profound implications. The stress-induced regression of pyramidal cell dendrites in the CA3 region of the hippocampus is mediated by adrenal corticosteroids, but the mechanisms underlying this effect are unclear. Hippocampal homeostasis depends on the balance between excitatory and inhibitory transmission mediated by glutamate and ā-aminobutyric acid (GABA), respectively. Glutamate has been implicated in the morphological actions of corticosterone (CORT), but the role of GABA has not been examined. The goal of these studies is to determine if positive modulators of $GABA_A$ receptors, such as benzodiazepines or steroids, protect against stress-induced dendritic atrophy. On a more mechanistic level, these studies will determine if adrenal steroids alter the expression of specific $GABA_A$ receptor subunits. Prolonged exposure to corticosterone might alter GABAergic synaptic inhibition, and in this manner modulate structural plasticity in the hippocampus relevant to learning and memory processes as well as clinical disorders.

Sally Schroeter, Ph.D., Emory University, School of Medicine, "Ontogeny of the Antidepressant-sensitive 5HT Transporter." The precise coordination of events responsible for embryonic morphogenesis relies on the faithful execution of intrinsic genetic programs, triggered and modified by extrinsic morphogens. In addition to its established role in synaptic signaling, 5-hydroxytryptamine (5HT or serotonin) may act as an embryonic morphogen. 5HT is present in mammalian embryos before serotonergic neurons mature, increases cell division, alters cell morphology, and modulates cell movements. 5HT is specifically accumulated by embryonic tissues in a manner analogous to the molecules sequestration at adult synapses. Notably, 5HT transport antagonists block embryonic 5HT accumulation and lead to craniofacial and heart abnormalities, suggesting that transport per se may regulate the morphogenetic potential of 5HT in the embryo. In the mouse embryo, a precocious and heterogeneous expression of transporter mRNAs has been identified with *in situ* hybridization, and 5HT transporter-specific antibodies have been used to correlate the location of 5HT transporter proteins with site identified by 5HT transport antagonists. These tools now permit the elucidation of the temporal and spatial distribution of 5HT transporters in the embryo as well as the inhibition of 5HT transporter gene expression in cultured cells, providing an interpretive framework for pharmacological manipulations of the transporter in development. Findings from these studies may reveal molecular mechanisms for the ability of drugs that bind to the 5HT transporter, such as antidepressants and cocaine, to cause birth defects.

Individuals who began their awards in July of 1993 are:

Holly Boettger-Tong, Ph.D., University of Texas Medical School.

Galina Kuznetsov, Ph.D., Dana-Farber Cancer Institute, Harvard University.

Song Song, M.D., Harvard University Medical School.

Those individuals entering the second year of their awards in 1993 are:

Eran Blaugrund, Ph.D., Columbia University, College of Physicians and Surgeons.

Stefan Strack, Ph.D., Vanderbilt University, School of Medicine.

Ending their awards in 1993 are:

Charles Allan Fox, Ph.D., Mental Health Research Institute, University of Michigan.

Sarath Kanekal, Ph.D., University of Texas School of Pharmacy—(one year award—ended June 1993).

Laura J. Sim, Ph.D., Department of Physiology and Pharmacology, Bowman Gray School of Medicine, Wake Forest University.

Marie Vivien St-Pierre, Ph.D., Department of Physiology, Tufts University School of Medicine.

TOXICOLOGIC-PATHOLOGY

Faculty Awards in Toxicologic-Pathology

Initiated in 1983, this award was developed to attract scientists interested in analyzing, reviewing and questioning, where appropriate, the present state of the art in the field of toxicology. With the concurrence of the Board, the Scientific Advisory Committee phased out this program after 1992 due its success in bringing talented individuals to the field of toxicologic-pathology. The goal of this program had been to support veterinary and comparative pathologists who would devote two years to research with drugs. The last award was made in 1992. The total number of awards made for this program is 18.

Ending her award in June of 1994:

Jan L. VanSteenhouse, D.V.M., Ph.D., Assistant Professor, Veterinary Clinical Pathology, Louisiana State University, School of Veterinary Medicine—"Toxicity of a Naturally Occurring Nitrile and the Role of Glutathione Metabolism in Toxicity."

Dr. Gertrude Elion, Nobel Prize Winner and Scientist Emeritus for the Wellcome Research Laboratories of Burroughs Wellcome Co., is warmly greeted by Foundation President Morry Bectel and Scientific Consultant Ed Cafruny, longtime friend Bob Parks of Brown University and Advisory Committee member Eddie Way. Dr. Elion delivered the Thomas E. Hanrahan Memorial Lecture at the PhRMA Foundation Annual Awardee Meeting, January 20, 1994, Washington, D.C.

PHARMACEUTICS

Undergraduate Research Fellowships in Pharmaceutics

This fellowship program, which began in 1990, is designed to encourage undergraduate students in pharmacy, chemistry, biology or a related discipline to pursue an advanced degree in pharmaceutics, thereby attempting to alleviate the current shortage of well-trained investigators in this vital discipline. The PhRMA Foundation hopes to accomplish this goal by providing support for the undergraduate student to participate in a meaningful research project with a motivated, inspiring and research-active pharmaceutics faculty member.

This award provides a selected pharmaceutics faculty member with a one-year, $5,000 fellowship which the faculty member can provide to a qualified undergraduate of his or her choosing. Eleven awards were made for 1994, bringing the total number of awards to 58.

Faculty and their undergraduate students who will receive fellowships between January and August 1994 are:

Hayat Alkan-Onyuksel, Ph.D., Associate Professor, Pharmaceutics and Pharmacodynamics
Student: Jennifer Lin—University of Illinois at Chicago College of Pharmacy "Interaction of Surfactant Monomers with Model Membranes"—This study will investigate the interaction between a surfactant and model membrane using a novel method, in order to understand how a penetration enhancer works to increase the bioavailability of a drug by oral route.

Janet P.F. Bai, Ph.D., Assistant Professor, Pharmaceutics Department
Student: Phuong Nam Tran—University of Minnesota, College of Pharmacy "Insulin-degrading Enzyme Limiting Insulin Absorption in the Lungs"—The long-term goal of the research is to achieve clinical pulmonary efficacy of insulin and to provide a convenient and nonpainful treatment for millions of diabetic patients. This research will delineate whether insulin-degrading enzyme (IDE) is the major enzyme limiting pulmonary insulin absorption.

M. J. Cho, Ph.D., Associate Professor
Student: Alice Karobia —University of North Carolina, Chapel Hill School of Pharmacy "ELISA Development for Determination of Mouse Anti-Chlamydia sIgA"—The development of a vaccine against chlamydia infection has been a daunting task mainly due to difficulty in inducing immunity in the body's mucus membranes. The development of an enzyme linked immunosorbent assay will help to determine the antibody level.

Jeffrey L. Fox, Ph.D., Associate Professor, Pharmaceutics and Pharmaceutical Chemistry
Student: Shane J. Colby—University of Utah, School of Pharmacy "The Effect of Solution Fluoride Ion on Dissolution of Cabonate Apatites"—This research will use the physical model approach to study the effect of solution fluoride ion on dissolution kinetics of carbonate containing apatites (CAP's). We have previously shown that the dissolution of hydroxyapatite and human dental enamel is governed by a CA_{10} $(PO_4)_6$ F_2 surface complex and we expect to be able to establish this for CAP's as well.

David J. W. Grant, D.Sc., Professor, Department of Pharmaceutics
Student: Ceaminia Sze-man Yuen—University of Minnesota, College of Pharmacy "Control and Prediction of Drug Hydrate Phase Crystallized From Water + Organic Solvent Mixtures"—Some drugs are prepared as solid hydrates by crystallizing the drug from an appropriate mixture of water with an organic co-solvent. This study will test a thermodynamic method for selecting and optimizing the composition of the solvent mixture for crystallizing any particular drug hydrate.

Vincent H. L. Lee, Ph.D., Professor and Chairman, Pharmaceutical Sciences
Student: Lan Ngoc Nguyen—University of Southern California, School of Pharmacy "Protein Transport Across Cultured Respiratory Epithelial Monolayers" —This research seeks to test the feasibility for enhancing the capture of protein drugs by cells in the trachea and alveoli so as to promote protein entry into the blood stream.

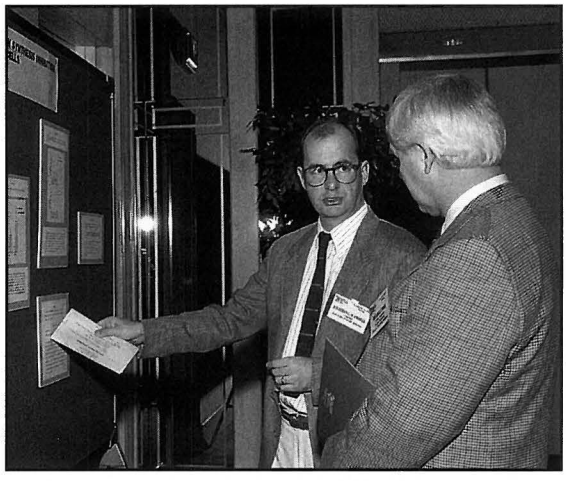
Clyde M. Ofner III, Ph.D., Associate Professor, Pharmaceutics Department
Student: Moon Sung Kim—Philadelphia College of Pharmacy and Science "Extended Delivery of Methotrexate from Biodegradable Gelatin Microspheres"—The focus of this research is to determine the feasibility of covalently conjugating low molecular weight therapeutic molecules to biodegradable microspheres to provide a long-term release and local effect. Methotrexate incorporation, *in vitro* release and microsphere degradation will be evaluated.

Gary M. Pollack, Ph.D., Associate Professor, Division of Pharmaceutics
Student: Sajel Patel—University of North Carolina, Chapel Hill, School of Pharmacy, "Developing Pharmacologic Strategies for Increasing Brain Tissue Exposure to Polar Drugs, Including Antivirals"—This project will be undertaken to determine the mechanism by which the anticonvulsant drug valporic acid increases the penetration of AZT into brain tissue. The results of this study may provide insight into useful methods to target drug delivery to the brain.

Philip C. Smith, Ph.D., Assistant Professor, Division of Pharmaceutics
Student: Christina Marie Seugling—University of North Carolina, Chapel Hill, School of Pharmacy "Futile Cycling of Acyl Glucuronides in Rats"—Acyl glucuronides are reactive metabolites that react irreversibly with proteins *in vivo*. The factors influencing *in vivo* exposure to these metabolites will be investigated by administration of the metabolites to rats. These studies should increase our understanding of whether "futile cycling" of acyl glucuronides is a common occurrence for the spectrum of compounds that form acyl glucuronides. Concurrent *in vitro* studies will examine what specific enzymes are responsible for the cleavage of acyl glucuronides.

Robert M. Straubinger, Ph.D., Assistant Professor, Department of Pharmaceutics
Student: Ruba Fayeq Husein—State University of New York, Buffalo, School of Pharmacy "Biopharmaceutics of Drug:Liposome Formulations for Therapy of Brain Tumors" —This research project is to develop and test novel drug:carrier formulations, and test their efficacy in a rat brain tumor model. The drug carrier system to be investigated is liposomes (phospholipid vesicles) which have recently made great strides in potential utility for human therapy.

Raj Suryanarayanan, Ph.D., Associate Professor, Pharmaceutics Department
Student: Thanh Vo—University of Minnesota, College of Pharmacy, "Low Temperature Powder X-ray Diffractometry"—The preparation of protein formulation often includes a freeze-drying step. Loss of potency during freeze-drying is often a serious problem. This research will use powder X-ray diffractometry to study this problem.



During the Poster Session, advisory committee members have an opportunity to discuss the research of current and former awardees. Here, advisory committee member Dr. Hugh Lewis (R), Dean of the Purdue University School of Veterinary Medicine, and awardee Jonathan Scammel, Ph.D., University of South Alabama College of Medicine, discuss Dr. Scammel's poster.

Fellowship for Advanced Predoctoral Training in Pharmaceutics

Initiated in 1987, this program's purpose is to assist candidates who have one or two years remaining in their predoctoral training—the time during which they are engaged in dissertation research.

The fellowship program provides a stipend of $12,000 a year for two years and $500 a year for incidentals directly associated with the preparation of the dissertation. Six awards were made for 1994 bringing the total number of awards made to 46.

Those who received fellowships beginning between January and July 1994 are:

Suzanne S. Y. Leung, University of Minnesota, College of Pharmacy (one year)—"The Implications of Chirality on the Physicochemical Properties of Nonsteroidal Antiinflammatory Drugs." Interactions between drug enantiomer with each other and with excipients may result in complications for drugs in which only one enantiomer has the desired pharmacological activity. Nonsteroidal antiinflammatory drugs, such as ibuprofen, fenoprofen, and flurbiprofen, will be used as model compounds to investigate the effects of those interactions on physicochemical and crystal properties. *Thesis Advisor:* Dr. David J. W. Grant, Professor of Pharmaceutics.

Shihong Li, University of Kansas, School of Pharmacy—"Protein Stability: Mechanistic Study of Methionine Oxidation." The objective of this research is to elucidate the mechanism of methionine oxidation in peptides and proteins by prooxidant/transition metal systems which are able to generate a variety of active oxygen species. This approach enables Dr. Li to mimic the oxidation condition which exists during protein drug processing and thus the results will help to develop oxidation resistant formulations. *Thesis Advisor:* Dr. Ronald Bochardt, Summerfield Distinguished Professor, Pharmaceutical Chemistry.

Lee M. Muraoka, Purdue University, School of Pharmacy and Pharmacal Sciences—"Effect of Glass Transition Temperature on the Stability of Freeze Dried Protein Formulations." In this research, the glass transition temperatures of model formulations of freeze-dried proteins will be systematically varied, and the quantitative relationship between stability, storage temperature, and glass transition temperature will be determined. *Thesis Advisor:* Steven L. Nail, Ph.D., Industrial and Physical Pharmacy.

David A. Putnam, University of Utah, College of Pharmacy—"Biorecognizable Polymers for Cancer Therapy: Structure-Property Relationships of Targetable Drug/Polymer Conjugates." Polymer/drug conjugates may be used to increase the efficacy and decrease the toxicity of anticancer compounds. The purpose of this project is to study biorecognizable polymeric prodrugs of anticancer agents and to determine the structure-property relationships associated with their cell surface and intracellular biorecognizability. *Thesis Advisor:* Jindrich Kopecek, D.Sc., Ph.D., Professor, Pharmaceutics.

Mark J. Rose, University of Kansas, School of Pharmacy—"The Development of Electrogenic Derivatization Reagents for the Bioanalysis of Amine Bearing Analytes." The development of technology applicable for the high sensitivity determination of peptides and peptide mimetics in biological solutions is an important research goal due to the increased number of these analytes being evaluated as drug candidates. Electrogenic derivatization reagents when used in conjunction with advanced separation techniques such as u-bore LC and Capillary Electrophoresis will serve to enhance quantitation of these amine containing molecules. This research will design and synthesize pre-separation electrogenic derivatizing reagents; evaluate the reactivity of the reagents with various amines; use these reagents in conjunction with HPLC or CE; and apply the technology to quantitative bioanalytical methodology. *Thesis Advisor:* John F. Stobaugh, Ph.D., Associate Professor of Pharmaceutical Chemistry.

Beth A. Szkudlarek, University of Michigan, College of Pharmacy—"Formulation and Process Control of the Selective Crystallization of Phosphate Buffer Components During Freezing." The freezing of phosphate buffer may cause selective salt precipitation, incurring a pH change. The goal of this research is to understand the kinetics of phosphate salt crystallization and the effects that additives have on both crystallization and stability of proteins in freeze-dried formulations. *Thesis Advisor:* John F. Stobaugh, Ph.D., Associate Professor of Pharmaceutical Chemistry.

Those who received fellowships in 1993 and continued 1994 are:

Kim Hancock, Purdue University, School of Pharmacy.

Huai-Hung Danny Kao, University of Kentucky, College of Pharmacy.

Sandy Koppenol, University of Wisconsin-Madison, School of Pharmacy.

Jason LePree, University of Wisconsin-Madison, School of Pharmacy.

Jeffrey David Lewis, Purdue University, School of Pharmacy and Pharmacal Sciences.

Carlos Noel Velez, University of North Carolina at Chapel Hill, School of Pharmacy.

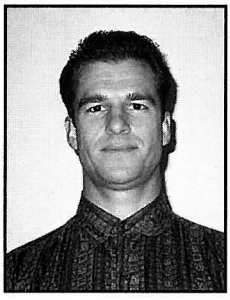
Wan-Ching Yen, University of Southern California, School of Pharmacy.

Conversing at the Annual Awardee Banquet are Lodewijk de Vink, President and Chief Operating Officer of Warner-Lambert and Chairman-Elect of the PhRMA Board, and Dr. Gertrude B. Elion, Thomas E. Hanrahan Memorial Guest Lecturer.

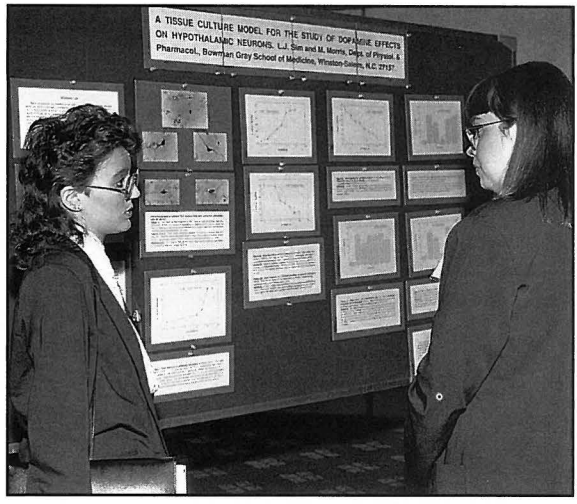
Postdoctoral Research Fellowships in Pharmaceutics

Complementing the other two pharmaceutics programs offered by the PhRMA Foundation, the Postdoctoral Research Fellowships in Pharmaceutics entered its third year. The purpose of this program is to encourage more qualified graduates to obtain the postdoctoral research training so vitally needed in the area of pharmaceutics. The PhRMA Foundation and its Pharmaceutics Advisory Committee, in recognizing the critical need for such well-trained scientific investigators, gives two awards in the amount of $25,000 per year for two years, totaling seven awards since inception.

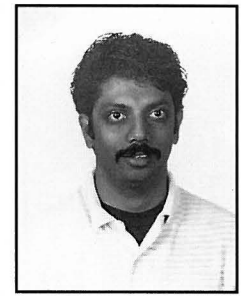
In 1994, the following individuals received awards:



Kenneth R. Phares, Ph.D., University of North Carolina, Chapel Hill, School of Pharmacy—"*In Vitro* Cell Monolayer Model for Investigating Folate Receptor-mediated Transcytosis." Folic acid is an essential vitamin that is required for normal cellular function, growth, and development. It is used therapeutically in clinical folate deficiency states. The carrier-mediated uptake of folic acid was found to be regulated by membrane-bound folate-binding moieties (Rothenberg, 1970). Reduced folates can enter cells by a carrier-mediated low-affinity (K_m = 1.5 ìM) anion-transport protein that is found in nearly all cells. However, folic acid and the reduced form in the serum, 5-methyltetrahydrofolate, are internalized via the FBP (Antony, 1992). This protein has been shown to bind folates with high affinity and deliver them into the cytoplasm by receptor-mediated endocytosis (Kane and Waxman, 1989). Uptake studies of methotrexate, the classical dihydrofolate reductase inhibitor, have demonstrated that most cultured cells can express FBP and the reduced folate carrier (Jansen *et al.*, 1990). Folic acid is believed to undergo rapid endocytosis via FBP in the presence of an extracellular folate concentration at or below a physiological level of 50 nM. This is in contrast to the carrier for reduced folate in cultured cells, which acquires folic acid in the presence of supraphysiological folate concentrations (Antony, 1992). The purpose of this research is to expand upon the knowledge of folate receptor-mediated endocytosis and elucidate the mechanism(s) by which folate undergoes transepithelial transport. Limited information is available regarding the overall process, and this transcytosis can be, at least in concept, exploited in delivering compounds that exhibit poor intestinal absorption. The development of a cell monolayer as a model of the intestinal mucosa would provide a unique opportunity to study both the apical and basolateral transport processes independently.



During the Poster Session, a current fellow in pharmacology/ morphology—Holly Boettger-Tong (l) of the University of Texas Medical School—and Dr. Laura Sim of the Bowman-Gray School of Medicine, a former fellow—are discussing aspects of Dr. Sim's research. The Poster Session offers a forum for awardees to share their research.



Srinivasan Venkatesh, Ph.D., University of Utah, School of Pharmacy —"Influence of Compositional and Morphological Heterogeneity on Equilibrium Distribution and Kinetics of Drug Transport in Parenteral Emulsions." Traditionally, parenteral lipid emulsions have been considered to be comprised of dispersed oil drops of various sizes stabilized by a monolayer of phospholipid. This view has recently been challenged. In addition to heterogeneity in particle size, emulsions are also heterogeneous with respect to composition (phospholipid/oil ratio) and morphology (number of phospholipid layers) of the oil droplets. Dr. Venkatesh's believes that this heterogeneity will strongly influence the equilibrium distribution of drugs and also their transport out of emulsion droplets, thereby affecting the solubility, stability and *in vivo* performance. The overall objective of this research is to study the influence of the compositional and morphological heterogeneity on drug intake and release from parenteral lipid emulsions.

Beginning their awards in 1993 are:

Jeffrey A. Hughes, Ph.D., University of North Carolina at Chapel Hill, School of Medicine.

Lawrence Ka-Yun Ng, Ph.D., University of Kansas, School of Pharmacy.

Entering the second year of their awards in 1993 are:

Prashant J. Chikhale, Ph.D., University of Kansas, School of Pharmacy.

Michael Mulski, Ph.D., Department of Chemical Engineering and Materials Sciences, University of Minnesota.

Raymond D. Skwierczynski, University of Wisconsin-Madison, Medical School.

RESEARCH GRANTS

An important aspect of the PhRMA Foundation effort has been the support of fundamental research. Since 1971 a change in emphasis within the Foundation shifted the bulk of the funds into educational support programs and, consequently, less into research. It is understood that these educational programs place high emphasis on the research programs of the applicants for each award. In this sense, educational support programs are in fact also supporting research. The Foundation continues to accept requests for research support and suggestions for pertinent research projects since it is important that the potential within the Foundation for helping that particularly promising effort be maintained.

The Foundation will continue to review research applications that do not fall within the scope of its formal programs, but will not fund them unless they are deemed to be exceptional and novel approaches that have not generated support from conventional sources.

ETHICAL CONSIDERATIONS

The Scientific Advisory Committee as well as the program advisory committees of the PhRMA Foundation are sensitive to the appropriate use of experimental subjects, animals and humans, in research. In their deliberations, they consider all aspects of a proposal and may deny support for many reasons. Careful consideration is given to humane use and care of animal subjects. For human and animal research, the project review committee requires, in writing, a statement of adherence to prevailing standards of ethical research practices, including Institutional Review Board approval before initiation of any research project. In addition, for human research, assurance of informed consent will be required.

RESEARCH STARTER GRANTS

Active since 1971, the Research Starter Grants are intended to provide financial support for beginning investigators. The program, in 1994, allowed for 17 research starter grants at $12,500 per year with the second year contingent upon need.

The first awards were made in 1972, and a total of 477 research starter grants have been made, including the 17 awards beginning January 1, 1994:

Recipients of the grants beginning January 1994 are:

John C. Chrivia, Ph.D.
St. Louis University
Health Sciences Center
School of Medicine

James G. Donnelly, Ph.D.
The Catholic University of America

Keith S. Elmslie, Ph.D.
Tulane University
School of Medicine

Henry C. Farrar, M.D.
University of Arkansas
College of Medicine

Ian S. Haworth, Ph.D.
University of Southern California
School of Medicine

Dale G. Hoyt, Ph.D.
University of Pittsburgh
School of Medicine

Calvin M. Johnson
University of Florida
College of Mecicine

Deanna L. Kroetz, Ph.D.
University of California, San Francisco
School of Pharmacy

Beth Levant, Ph.D.
University of Kansas
School of Medicine

Ming Li, Ph.D.
University of South Alabama
School of Medicine

Grace K. Pavlath, Ph.D.
Emory University
School of Medicine

Michael E. Ritchie, M.D.
University of Cincinnati
College of Medicine

James W. Sharp, D.V.M., Ph.D.
Kansas State University

Michael W. Smar, Ph.D.
South Dakota State University

Paul M. Stemmer, Ph.D.
University of Nebraska
College of Medicine

Carston R. Wagner, Ph.D.
University of Minnesota Medical School

T. Mark Zabriskie, Ph.D.
Oregon State University
College of Pharmacy

Based on need for funds, a review of the 20 research starter grantees whose awards began January 1, 1993, for a second year of the awards resulted in 12 of them having their awards continued. These are:

Robin Humcke Bogner, Ph.D.
University of Connecticut
School of Pharmacy

Kathleen M. Boje, Ph.D.
State University of New York, Buffalo
College of Pharmacy

Richard A. Gibbs, Ph.D.
Wayne State University
College of Pharmacy and Allied Health Professions

Anne L. Killam, Ph.D.
Michigan State University
College of Human Medicine

Ah-Ng Tony Kong, Ph.D.
Jefferson Medical College
Thomas Jefferson University

Mark Leid, Ph.D.
Oregon State University
College of Pharmacy

Nancy Jo Leidenheimer, Ph.D.
Louisiana State University
School of Medicine in Shreveport

Wendi S. Neckameyer, Ph.D.
Saint Louis University
School of Medicine

William H. Percy, Ph.D.
University of South Dakota
School of Medicine

William C. Sessa, Ph.D.
Yale University
School of Medicine

Jeffrey Dennis Steketee, Ph.D.
Louisiana State University
School of Medicine in Shreveport

Mark R. Walter, Ph.D.
University of Alabama at Birmingham
School of Medicine

PURPOSE

The PhRMA Foundation was established to promote the betterment of public health through scientific and medical research, with particular reference to the study and development of the science of therapeutics. In achieving this goal, the Foundation plans and initiates scientific and medical research activities, collects and disseminates the results of these activities, and provides financial support and aid to individuals or institutions whose purposes are scientific, educational or charitable.

Certain guidelines have been developed to promote the wise and proper use of the limited resources available. The areas of interest which govern the distribution of funds are in support of fundamental research on drugs and programs for training personnel in basic and clinical pharmacology, toxicology and pharmaceutics.

Throughout the year, programs have been supported and developed which provide the means of achieving the goals of the Foundation. Many worthwhile proposals have been submitted. It has been necessary to limit support to those who hold the highest promise of advancing the purposes of the Foundation.

Those areas not supported within the existing guidelines are:

(1) Research on specific drugs, unless the drug is for an orphan disease. This exclusion is not meant to preclude support of projects which, of necessity use a number of drugs to establish a methodology or screening program of potential general applicability. It does exclude those efforts primarily aimed at learning more about specific drugs or classes of drugs.

(2) Funds for construction. The Foundation is not unmindful of the needs and the tremendous pressures for private funds for construction projects. However, it is believed that the scientific community can be better served by channeling the Foundation's available resources into other areas.

(3) Funds for travel (except as otherwise indicated).

(4) Funds to cover entertainment costs.

While Foundation support of research continues, such support is currently primarily available in programs such as the Research Starter Grants as discussed on page 32 and under the Education and Training Programs Section on page 9.

While meetings have never received a large portion of the support dollar, only in very exceptional circumstances will meetings receive support in the future.

REPORT OF THE TREASURER

Robert C. Black
Secretary-Treasurer, Pharmaceutical Research and Manufacturers of America Foundation

Since its inception in 1965, the PhRMA Foundation has been supported by the generosity of the research-intensive pharmaceutical manufacturers—the PhRMA member firms, associates and research affiliates. The total income of the Foundation in 1993 was $2,528,689. Of this amount, $2,337,250 came from contributions. The balance of $191,439 came from investments and refunds of unexpended balances from grants.

In 1993, grants totaled $1,955,363; Foundation Annual Awardee Meeting and ASPET meeting amounted to $86,128; Honoraria and Professional Services totaled $85,620; Committee Meetings amounted to $84,929; special projects and other expenses for 1993 amounted to $407,706. The total fund balance as of December 31, 1993 was $5,162,691. This figure, however, does not reflect the tentatively authorized, undisbursed funds for some of the grants and programs described earlier. The Foundation reports these amounts as expenditures when the funds are disbursed. As of December 31, 1993, the contingency liability for 1994-97 was approximately $3,463,752.

The Foundation's financial position as of December 31, 1993, has been audited by the Washington D.C. accounting firm of Buchanan & Company.

Robert C. Black
Secretary-Treasurer
PhRMA Foundation
and
President
Zeneca Pharmaceuticals Group

Statement of Income and Expenditures For the Year Ended December 31, 1993

Income	
Contributions	2,337,250
Interest from investments	86,149
Interest Transferred from Future Commitment Fund	68,517
Miscellaneous Income	37,773
Total Income	**2,528,689**
Expenditures	
Grants (Note A)	
Clinical Pharmacology Unit Award	116,200
Faculty Awards in Clinical Pharmacology	370,000
Faculty Awards in Basic Pharmacology	84,758
Fellowships for Careers in Clinical Pharmacology	74,518
Advanced Predoctoral Fellowships in Pharm/Tox	276,000
Pharmacology-Morphology Fellowships	173,387
Medical Student Research Fellowships	75,000
Research Starter Grants	340,000
Faculty Awards in Toxicologic-Pathology	60,000
Advanced Predoctoral Fellowships in Pharmaceutics	128,000
Undergraduate Fellowships in Pharmaceutics	45,000
Postdoctoral Fellowships in Pharmaceutics	112,500
Grant Total	1,955,363
Administrative	
Annual Awardee Meeting and ASPET Meeting	86,128
Committee Meetings and Travel	84,929
Special Projects	11,784
Honoraria and Professional Services	85,620
Publications	61,842
Office Expense	58,237
Rent, Salaries, Taxes	275,843
Administrative Total	664,383
TOTAL EXPENDITURES	2,619,746
Excess of income over expenditures	(91,057)
Operating fund balance at January 1, 1992	2,940,381
Operating fund balance December 31, 1992	2,849,324
Future Commitment Fund (Reserve Fund) (Note B)	2,313,367
Total fund balance at December 31, 1992	**5,162,691**

Note A—In addition to the amounts shown, the Foundation is committed, subject to annual review, to make certain grants. At December 31, 1993, the amounts still to be disbursed with respect to these grants amounted to aggregated $3,463,752 with $1,903,029 of this to be disbursed during 1994; $1,146,823 in 1995; $353,900 in 1996; and $60,000 in 1997.

Note B—The Future Commitment Fund is a reserve fund established by the Foundation to ensure the continuation of existing grants.

Income from Investments	125,378
Interest Transferred to Operating Fund	(68,517)
Dividend Income	3,436
Gain (Loss) on Sale of Stock	76,972
Less: Trust Commission Expense	5,090
Excess of expenditures over income:	**132,179**
Future Commitment Fund Balance at January 1, 1993	2,181,188
Future Commitment Fund Balance at December 31, 1993	**2,313,367**

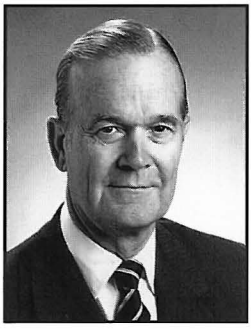
ORGANIZATION AND ADMINISTRATION

The PhRMA Foundation operates through its officers, Board of Directors and six advisory committees. In May of 1994, Charles A. Sanders, M.D., Chairman of Glaxo Inc., was re-elected Chairman. Philip R. Tracy, President and Chief Executive Officer of Burroughs Wellcome Co., was re-elected Vice-Chairman, and Mr. Robert C. Black, President of Zeneca Pharmaceuticals Group, was re-elected Secretary-Treasurer.

Maurice Q. Bectel, D.Sc., again served as the Foundation's President. Donna Moore served as Director of Programs, and Edward J. Cafruny, M.D., Ph.D., and C. Joseph Stetler, Esq., continued to serve as Foundation consultants —Dr. Cafruny as scientific consultant and Mr. Stetler as staff counsel. Mr. Stetler, who was the first President of the Foundation and instrumental in the operations of the Foundation since its beginning, retired as Consultant on June 30, 1994.

Dr. Charles Sanders (left), Chairman of the PhRMA Foundation Board greets current PhRMA and PhRMA Foundation Board members after the Annual Awardee Banquet—(l to r) Robert C. Black, President of Zeneca Pharmaceuticals Group and PhRMA Foundation Secretary-Treasurer; Philip R. Tracy, President and Chief Executive Officer, Burroughs Welcome Co., and PhRMA Foundation Vice-Chairman of the Board; G. Gilbert Cloyd, Vice President, Pharmaceuticals, Procter & Gamble USA, The Procter & Gamble Company.

1994-95 Officers



Charles A. Sanders, M.D.
Chairman
PhRMA Foundation
Chairman
Glaxo Inc.
Research Triangle Park,
North Carolina

Philip R. Tracy
Vice Chairman
PhRMA Foundation
President and Chief Executive Officer
Burroughs Wellcome Co.
Research Triangle Park, North
Carolina

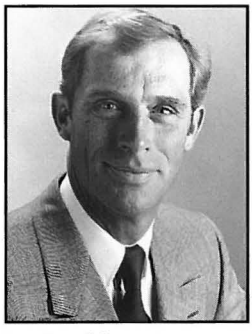
Robert C. Black
Secretary-Treasurer
PhRMA Foundation
President
Zeneca Pharmaceuticals Group
Wilmington, Delaware

Maurice Q. Bectel, D.Sc.
President
PhRMA Foundation
Washington, DC

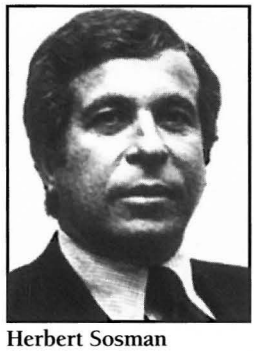
1994-95 Board of Directors

***Gordon M. Binder**
Chairman and Chief Executive Officer
Amgen
Thousand Oaks, California

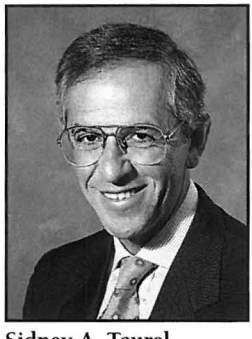
G. Gilbert Cloyd
Vice President, Pharmaceuticals
Procter & Gamble USA
The Procter & Gamble Company
Cincinnati, Ohio



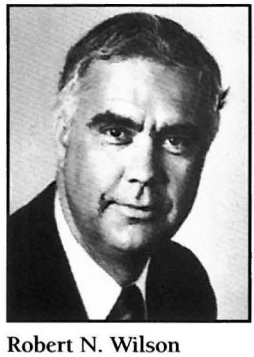
Jan Leschly
Chief Executive
SmithKline Beecham
Philadelphia, Pennsylvania



Herbert Sosman
President
Wallace Laboratories
Carter-Wallace, Inc.
Cranbury, New Jersey



Sidney A. Taurel
Executive Vice President and President, Pharmaceutical Division
Eli Lilly and Company
Indianapolis, Indiana



Robert N. Wilson
Vice Chairman, Board of Directors
Johnson & Johnson
New Brunswick, New Jersey

---

* *joined the Foundation Board in February '94*

***Patrick J. Zenner**
President and Chief Executive Officer
Hoffmann-La Roche Inc.
Nutley, New Jersey

Gerald J. Mossinghoff
President
Pharmaceutical Research and
Manufacturers of America
Washington, D.C.
(Ex-Officio)

Staff and Staff Consultants

C. Joseph Stetler, Esq.
Attorney at Law

Edward J. Cafruny, M.D., Ph.D.
Distinguished University Professor
University of Medicine and Dentistry
of New Jersey

Donna Moore
Director of Programs

---

* *joined the Foundation Board in December '93*

ADVISORY COMMITTEES

Scientific Advisory Committee

William R. Darrow, M.D., Ph.D.
(Chairman)
Senior Vice President
Medical Operations
Schering-Plough Corporation
Kenilworth, New Jersey

Paul Calabresi, M.D.
Chairman and Professor
Department of Medicine
Brown University
Providence, Rhode Island

Michael D. Gershon, M.D.
Professor and Chairman
Department of Anatomy & Cell Biology
Columbia University
College of Physicians and Surgeons
New York, New York

Jerry R. Mitchell, M.D., Ph.D.
President
Upjohn Laboratories
and
Vice Chairman of the Board
The Upjohn Company
Kalamazoo, Michigan

Frank Standaert, M.D.
Special Expert
Scientific Policy
National Institute of Mental Health
National Institutes of Health
Rockville, Maryland

James Swarbrick, D.Sc., Ph.D.
Vice President
Research and Development
AAI, Inc.
Wilmington, North Carolina

W. Leigh Thompson, Jr., M.D., Ph.D.
Chief Scientific Officer
Eli Lilly and Company
Indianapolis, Indiana

Hugh H. Tilson, M.D., Dr.P.H.
Vice President
International Surveillance Epidemiology and Economics Research
Burroughs Wellcome Co.
Research Triangle Park, North Carolina

Irwin M. Weiner, M.D.
Dean
College of Medicine
State University of New York, Brooklyn
Health Science Center
Brooklyn, New York

---

* *Frederick M. Radzialowski, Ph.D., retired as Chairman of the SAC in 1993 having served since 1989.*

Clinical Pharmacology Advisory Committee

Paul Calabresi, M.D.
(Chairman)
Chairman and Professor
Department of Medicine
Brown University
Providence, Rhode Island

***Darrell R. Abernethy, M.D., Ph.D.**
Francis Cabell Brown Professor of
Medicine and Pharmacology
and
Director
Division of Clinical Pharmacology
School of Medicine
Georgetown University
Washington, D.C.

Terrence F. Blaschke, M.D.
Professor of Medicine and
Pharmacology
Division of Clinical Pharmacology
Stanford University
School of Medicine
Stanford, California

Edward A. Carr, Jr., M.D.
Emeritus Professor
SUNY at Buffalo
Buffalo, New York

Leo E. Hollister, M.D.
Professor of Psychiatry and
Pharmacology
and
University of Texas/Houston
Medical Director
Harris County Psychiatric Center
Houston, Texas

Louis Lemberger, M.D., Ph.D.
Professor of Pharmacology,
Medicine and Psychiatry
School of Medicine
Indiana University
Indianapolis, Indiana

Gilbert Mannering, Ph.D.
Professor Emeritus
Department of Pharmacology
University of Minnesota
Medical School
Minneapolis, Minnesota

***Alan B. Nies, M.D.**
Executive Director
Clinical Pharmacology
Merck & Co., Inc.
Rahway, New Jersey

Lester E. Soyka, M.D.
Vice-President
Human Pharmacology and
International Clinical Research
Bristol-Myers Squibb Co.
Princeton, New Jersey

---

* *joined the Committee in 1994*

** *William B. Abrams, M.D., former Executive Director for Scientific Development, Merck, Sharp and Dohme Research Laboratories, and Dr. Albert Sjoerdsma, M.D., Ph.D., President Emeritus, Marion Merrell Dow Research Institute, retired from the Clinical Pharmacology Advisory Committee in 1994. Dr. Abrams had served on the Committee for ten years. Dr. Sjoerdsma had served on the Committee for 25 years.*

Basic Pharmacology Advisory Committee

Irwin M. Weiner, M.D.
(Chairman)
Dean, College of Medicine
State University of New York
Brooklyn, New York

James W. Aiken, Ph.D.
Director
Endocrine Pharmacology and Metabolism
The Upjohn Company
Kalamazoo, Michigan

Terry L. Bowlin, Ph.D.
Director
Department of Immunology
Marion Merrell Dow Research Institute
Cincinnati, Ohio

Theodore M. Brody, Ph.D.
Professor and Former Chairman
Department of Pharmacology and Toxicology
Michigan State University
East Lansing, Michigan

George C. Fuller, Ph.D.
Dean and Professor of Pharmacology
College of Pharmacy and Allied Health Professions
Wayne State University
Detroit, Michigan

James R. Gillette, Ph.D.
Former Chief, Laboratory of Chemical Pharmacology
National Heart, Lung & Blood Institute
National Institutes of Health
Bethesda, Maryland

Keith F. Killam, Jr., Ph.D.
Professor and Former Chairman
Department of Medical Pharmacology
University of California, Davis
School of Medicine
Davis, California

George R. Lenz, Ph.D.
Andover, Massachusetts

Bernard L. Mirkin, M.D., Ph.D.
William G. Swartchild, Jr. Distinguished Chair in Research
Head and Director of Research
Children's Memorial Institute for Education and Research
Professor of Pediatrics
Northwestern University Medical School
Chicago, Illinois

Robert E. Parks, Jr., M.D., Ph.D.
E. E. Brintzenhoff Professor of Medical Science
Division of Biology and Medicine
Brown University
Providence, Rhode Island

Sidney Pestka, M.D.
Professor and Chairman
Department of Molecular Genetics and Microbiology
University of Medicine & Dentistry of New Jersey
Robert Wood Johnson Medical School
Piscataway, New Jersey

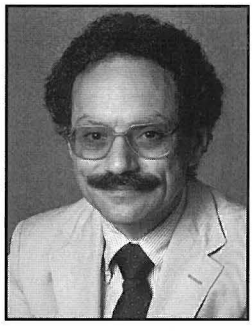
Frederick M. Radzialowski, Ph.D.
President
FMR Research Associates
Glenview, Illinois

Frank Standaert, M.D.
Special Expert
Scientific Policy
National Institute of Mental Health
National Institutes of Health
Rockville, Maryland

Dhiren R. Thakker, Ph.D.
Director
Department of Drug Metabolism
Research Institute
Glaxo Inc.
Research Triangle Park,
North Carolina

E. Leong Way, Ph.D.
Professor Emeritus of
Pharmacology, Toxicology
and Pharmaceutic Chemistry
Schools of Medicine and Pharmacy
University of California, San
Francisco
San Francisco, California

Pharmacology-Morphology Advisory Committee



Michael D. Gershon, M.D.
(Chairman)
Professor and Chairman
Department of Anatomy & Cell
Biology
Columbia University
College of Physicians & Surgeons
New York, New York

George A. Condouris, Ph.D.
Professor and Former Chairman
Department of Pharmacology
University of Medicine and
Dentistry of New Jersey
Newark, New Jersey

Cheryl Dreyfus, Ph.D.
Associate Professor
Department of Neuroscience &
Cell Biology
University of Medicine and
Dentistry of New Jersey
Robert Wood Johnson Medical
School
Piscataway, New Jersey

James A. Ferrendelli, M.D.
Professor of Pharmacology and
Neurology
Department of Neurology and
Neurological Surgery
School of Medicine
Washington University
St. Louis, Missouri

Felix A. de la Iglesia, M.D.
Vice President
Pathology & Experimental
Toxicology
Parke-Davis Pharmaceutical
Research
Ann Arbor, Michigan

Robert B. Jennings, M.D.
James B. Duke Professor of
Pathology
School of Medicine
Duke University
Durham, North Carolina

**Hugh B. Lewis, B.V.M.S.,
M.R.C.V.S.**
Dean, School of Veterinary
Medicine
Purdue University
West Lafayette, Indiana

***David L. G. Nelson**
Senior Research Scientist
Lilly Research Laboratories
A Division of Eli Lilly and Company
Indianapolis, Indiana

Lawrence M. Pinkus, Ph.D.
Scientific Review Administrator
Division of Research Grants
National Institutes of Health
Bethesda, Maryland

Henry J. Ralston III, M.D.
Professor and Chairman
Department of Anatomy
School of Medicine
University of California, San Francisco
San Francisco, California

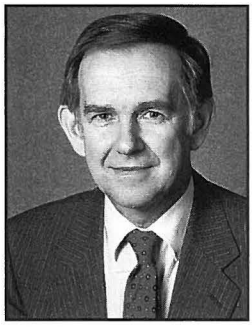
Leonard L. Ross, Ph.D.
President, Chief Executive Officer and Annenberg Dean
Medical College of Pennsylvania
Philadelphia, Pennsylvania

---

* *joined the Committee in 1994*

** *Dr. George D. Lumb, Scholar in Residence of Duke University Medical Center, and Professor Emeritus of Hahnemann University, College of Medicine retired from the Committee in 1994.*

Pharmaceutics Advisory Committee



James Swarbrick, D.Sc., Ph.D.
(Chairman)
Vice President
Research and Development
AAI, Inc.
Wilmington, North Carolina

William I. Higuchi, Ph.D.
Distinguished Professor and Chairman
Department of Pharmaceutics
College of Pharmacy
University of Utah
Salt Lake City, Utah

Douglas Mendenhall, Ph.D.
Vice President
Pharmaceutical Development
Glaxo Inc.
Research Triangle Park, North Carolina

***Lynda M. Sanders, Ph.D.**
Director, Center for Drug Delivery Research
Syntex Laboratories, Inc.
Palo Alto, California

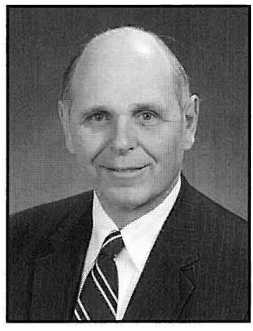
George Zografi, Ph.D.
Professor of Pharmaceutics
School of Pharmacy
University of Wisconsin-Madison
Madison, Wisconsin

---

* *joined the Committee in 1994*

** *Anthony A. Sinkula, Ph.D., formerly with The Upjohn Company, retired from the Committee in 1993.*

*Pharmacoeconomics Advisory Committee



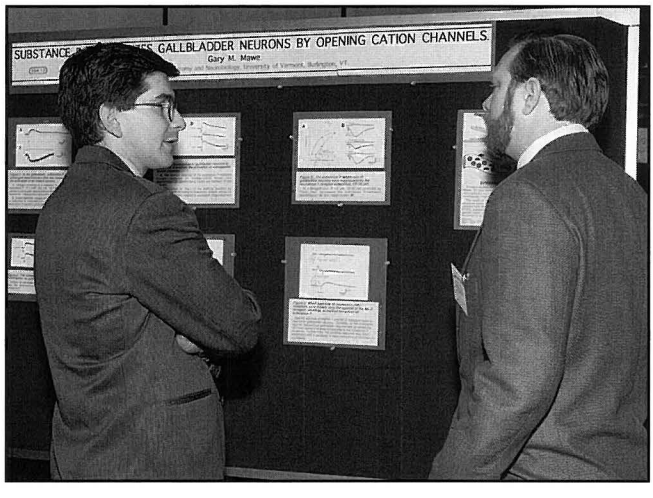
Hugh H. Tilson, M.D., Dr.P.H.
(Chairman)
Vice President
International Surveillance,
Epidemiology and Economics
Research
Burroughs Wellcome Co.
Research Triangle Park,
North Carolina

Lyle Bootman, Ph.D.
Dean
College of Pharmacy
University of Arizona
Tucson, Arizona

Jean Paul Gagnon, Ph.D.
Director of Industry Affairs
Marion Merrell Dow Inc.
Kansas City, Missouri

Raymond Townsend, Pharm.D.
Vice President
Applied Health Care Research
Glaxo Inc.
Research Triangle Park,
North Carolina

First program to be initiated in 1995.



Dr. Gary Mawe (r), former pharmacology/ morphology awardee, and Dr. Elias Lolis, a 1993 faculty awardee, discuss Dr. Mawe's research at the Poster Session.

BENEFACTORS

PhRMA MEMBER COMPANIES AND COMPANY FOUNDATIONS

Over $3 Million

*Bristol-Myers Squibb Foundation
(Bristol-Myers Squibb Company)

Over $2 Million

*Hoffmann-La Roche Inc.
*The Merck Company Foundation
(Merck & Co, Inc.
Merck Human Health Division)
*Warner-Lambert Foundation
(Warner-Lambert Company)
Parke-Davis

Over $1 Million

*The Upjohn Company
*Eli Lilly and Company Foundation
*SmithKline Beecham Foundation
SmithKline Beecham
SmithKline Beecham Animal Health
SmithKline Beecham Pharmaceuticals
SmtihKline Beecham Consumer Brands
SmithKline Beecham Clinical Laboratories
*Pfizer Inc.
*American Home Products Corporation
Wyeth Ayerst International, Inc.
Wyeth-Ayerst Laboratories
*Abbott Laboratories Fund
(Abbott Laboratories)
*Johnson & Johnson
Advanced Care Products, Inc.
Chicopee
Codman & Shurtleff, Inc.
Critikon, Inc.
Ethicon, Inc.
Immunobiology Research Institute, Inc.
Iolab Corporation
Janssen Pharmaceutica, Inc.
Johnson & Johnson Consumer Products, Inc.
Johnson & Johnson Health Management Inc.
Johnson & Johnson Hospital Services Inc.
Johnson & Johnson Interventional Systems, Inc.
Johnson & Johnson Medical, Inc.
Johnson & Johnson Professional, Inc.
Johnson & Johnson Professional Diagnostics, Inc.
LifeScan, Inc.
McNeil Consumer Products, Inc.
McNeil Pharmaceutical Co.
Noramco, Inc.
Ortho Diagnostic Systems Inc.
Ortho-McNeil Pharmaceutical Corporation

* *Contributor for 1993*

R. W. Johnson Research Institute
Personal Products Company
Therakos, Inc.
Vistakon, Inc.
*Searle
Searle Pharmaceutical Group
*Ciba-Geigy Corporation
Ciba Pharmaceuticals Division
*Schering-Plough Foundation, Inc.
*Glaxo Inc.

Over $500,000

*Burroughs Wellcome Co.
*Lederle Laboratories
Division of American Cyanamid Company
*Sterling Winthrop Inc.
Sanofi Winthrop
Sterling Winthrop Pharmaceutical Research Division
*Marion Merrell Dow, Inc.
*Zeneca Pharmaceutical Group

Over $250,000

*Sandoz Pharmaceuticals Corporation
Sandoz Corporation
*Syntex Corporation
Syntex Laboratories, Inc.
*Boehringer Ingelheim Corporation
Boehringer Ingelheim Pharmaceuticals, Inc.
Roxane Laboratories Inc.
*Miles Foundation (Miles Inc.)
*Carter-Wallace, Inc.
Wallace Laboratories
Wampole Laboratories
*Hoechst-Roussel Pharmaceuticals Inc.
Hoechst-Celanese Corporation
*Dupont Merck Pharmaceutical Company
*Procter & Gamble Company
*Rhone-Poulenc Rorer

Over $100,000

*3M Pharmaceuticals
*Berlex Laboratories

Under $100,000

*Knoll Pharmaceutical Company
*Organon Inc.
Astra USA, Inc.
Connaught Laboratories, Inc.
*Anaquest, Inc.
Reed & Carnrick
Allergan, Inc.
Genentech, Inc.
Fisons Corporation
Solvay Pharmaceuticals
*Alza Corporation
*Boots Pharmaceuticals Inc.
*B. F. Ascher & Company, Inc.

PhRMA ASSOCIATES AND RESEARCH AFFILIATES

Banner Gelatin Products
*Bozell Worldwide, Inc.
Cahners Publishing Company
*Frank J. Corbett, Inc.
IMS America LTD
Institute for Biological Research and Development, Inc.
Kallir, Philips, Ross, Inc.
Klemtner Advertising Inc.
Lavey/Wolff/Swift, Inc.
William Douglas McAdams, Inc.
Medical Economics Publishing Company, Inc.
*Medical Publishing EnterPrises
Medicus Intercon Internationals, Inc.
Nova Pharmaceuteical Corporation
*Ohmeda
*Scott-Levin Associates, Inc.
*Sudler & Hennessey Inc.
Triton Biosciences and Viacom/FCB

* *Contributor for 1993*

APPLICATIONS

Descriptive brochures and application forms for all of the PhRMA Foundation Grant Programs listed on the inside back cover are available by contacting the Foundation offices.

Also, as part of pursuing its objective of promoting careers in biomedical research, the Foundation accepts requests for support and suggestions for pertinent research projects outside the formal grant programs from qualified institutions and individuals. These grant applications are reviewed by members of the Foundation's Scientific Advisory Committee to ensure that the application falls within Foundation grant program guidelines and to identify qualified individuals and projects.

For more information:

Maurice Q. Bectel, D.Sc.
President, Pharmaceutical Research and
Manufacturers of America Foundation
1100 Fifteenth Street, N.W.
Washington, D.C. 20005

(202) 835-3470
(202) 467-4823 (fax)

PhRMA Foundation Current Programs for 1995

Name of Program/ Year of First Awards	Number of Awards Budgeted Yearly/ Length of Award	Program Budget	Deadline Announcement Date Starting Time
Clinical Pharmacology Advisory Committee			
(1) Faculty Awards in Clinical Pharmacology (1967)	3 budgeted/ 3 years	$ 360,000 total $ 40,000 per award per year	October 1 December 15 July 1
(2) Fellowships for Careers in Clinical Pharmacology (1973)	3 budgeted/ 2 years	$ 144,000 total $ 24,000 per award per year	October 1 December 15 July 1
(3) Medical Student Research Fellowships (1974-Amended 1982)	5 budgeted/ 3 months to 24 months	$ 50,000 total $ 833 per month maximum $ 10,000	January 15 March 15 July 1
Basic Pharmacology Advisory Committee			
(4) Faculty Awards in Basic Pharmacology/Toxicology (1973)	2 budgeted/ 2 years	$ 120,000 total $ 30,000 per award per year	September 15 December 15 July 1
(5) Research Starter Grants (1972)	13 budgeted/ 2 years	$ 325,000 total $ 12,500 per award per year	September 1 December 15 January 1
(6) Advanced Predoctoral Fellowships in Pharmacology/Toxicology (1978)	10 budgeted/ 1 or 2 years	$ 250,000 total $ 12,500 per award per year	September 15 December 15 January-August
Pharmacology-Morphology Advisory Committee			
(7) Fellowships in Pharmacology-Morphology including Cell Biology (1968)	3 budgeted/ 2 years	$ 129,000 total $ 21,500 per award per year	January 15 March 15 July 1
Pharmaceutics Advisory Committee			
(8) Advanced Predoctoral Fellowships in Pharmaceutics (1987)	5 budgeted/ 1 or 2 years	$ 125,000 total $ 12,500 per award per year	October 1 December 15 January-August
(9) Undergraduate Research Fellowships in Pharmaceutics (1990)	10 budgeted/ 1 year	$ 50,000 total $ 5,000 per award	October 1 December 15 January-July
(10) Postdoctoral Fellowships in Pharmaceutics (1992)	1 budgeted/ 1 or 2 years	$ 50,000 total $ 25,000 per award per year	October 1 December 15 January-December
Pharmacoeconomics Advisory Committee			
(11) Faculty Awards in Pharmacoeconomics (1995)	2 budgeted/ 2 years	$ 160,000 total $ 40,000 per award per year	September 1 December 15 July 1

All of the above programs will accept applications for research on drugs for rare diseases

Pharmaceutical Research and
Manufacturers of America Foundation
1100 Fifteenth Street, NW
Washington, DC 20005