CELEBRATING 30 YEARS

Dedicated to The Foundation's Benefactors

# 1995 ANNUAL REPORT

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Pharmaceutical Research and Manufacturers of America Foundation











# In Memory





Celebrating 30 Years



Frank G. Standaert, member of the Foundation's Basic Pharmacology Advisory Committee and Scientific Advisory Committee, died unexpectedly of a heart attack on March 17, 1995. Frank accomplished momentous achievements in the discipline of pharmacology and was a faithful colleague and devoted family man.

Graduated from Harvard with an A.B. cum laude in 1951, Frank went on to Cornell University Medical College where he received his M.D. in 1955. After an internship at The Johns Hopkins University Hospital, he served as a Lieutenant at the Naval Medical Research Institute from 1957 to 1959, after which he joined the faculty of the Department of Cornell where he remained until 1967. He was then appointed Professor and Chairman of the Department of Pharmacology at Georgetown University's School of Medicine. His personal charisma brought cohesiveness which served to strengthen the department for years to come. In 1987, Frank left Georgetown to become Vice President and Dean at the Medical College of Ohio in Toledo. In 1990 he became Director of Research at the Toledo Hospital. Frank served in many capacities within ASPET and as its President from 1991 to 1992. At his death, he was commuting to Washington, D.C. as a special expert to the National Institutes of Mental Health.

An accomplished and productive neuroscientist working in the pharmacology of agents which act at the neuromuscular junction, Frank published more than 100 papers on the physiology of agents used in anesthesia.

Anyone who knew Frank knew of his splendid sense of humor, as well as his devotion to teaching which, of course, endeared him to his students and to his colleagues as well. In performing reviews for the Foundation, he was meticulous in every detail. With enthusiasm and commitment, he carefully scrutinized each application in order to make sure every significant detail was brought to the attention of the review committee and that every applicant received a fair review. His ability to call up pertinent facts was incredible. His willingness to take charge of a situation and move forward to action was exceptional.

For 22 years Frank served on the Foundation's Basic Pharmacology Advisory Committee and when asked for his expertise in serving on the Scientific Advisory Committee in 1991, he readily accepted. His strength of character, his warm personality and his commitment served as a role model for us all. We will miss him greatly.

Frank leaves his wife of 36 years–Joan–and three sons, David (M.D., Ph.D.), Robert (Ph.D.) and Christopher (M.D.). A memorial fund has been established by ASPET to perpetuate his role in pharmacology. Those who wish to participate may forward their designated contribution to ASPET.

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Celebrating 30 Years

# Report of the Chairman



Sometimes, dramatic numbers creep up on a person, rather than jump out as being obvious. Such is the case with the PhRMA Foundation's grant programs, now approaching 30 years in operation, in some cases. An aggregate of \$40 million has been awarded, through the very competitive grant review process, and has assisted nearly 2,000 bright young scientific researchers in getting their careers underway. I believe the track record of the PhRMA Foundation is dramatic; one in which many can take pride.

We are mid-way through 1995 as this is being written and just a brief period of time since the U.S. pharmaceutical industry

completed the trauma of eliminating some 42,000 positions. Depending on the point of view, the industry was either "down-sizing" or "right-sizing," but, in either case, the industry had little choice but to respond to numerous wrenching pressures in search of economic efficiencies.

Some might contend that the industry has gone through a cyclical change, experiencing contraction, to be soon followed by growth, followed by yet another contraction. Still others contend that the industry has undergone a truly structural change—the supporters of "right-sizing"—and is currently replacing normal attrition needs. Whatever the case is in actuality, the need for highly trained and educated biomedical researchers and technical experts in a variety of disciplines throughout the pharmaceutical industry is real. And that's where the PhRMA Foundation makes its major contribution.

No one is unaware of the recent, and continuing, cutbacks in the scope and funding of a wide variety of projects by the federal government. Research and development funding traditionally supported through grants from the National Institutes of Health have not been spared. As NIH funding becomes more scarce, private sector funding sources—of which the Foundation is a major player—become increasing important.

And the "privatizing" of such financial support (to use the term in an unusual, but appropriate, context) is requiring the Foundation to critically examine its mission. While the review process is not yet completed, we are working on a revised Foundation Mission Statement as we position the Foundation for the next decade. Emphasis in this revised Mission will be placed on such principles as "maintaining American leadership" in developing biomedical technology by "supporting scientific and medical research efforts" and assisting in the development of young scientists' careers. The Foundation's Scientific Advisory Committee, with its breadth and length of experience, will advise the Board in developing this statement and we anticipate that the review process will be completed within the year. The change from the Foundation's historical role may not be dramatic, but prudent management requires a periodic review of the organization's objectives, and it is not uncommon for goal adjustments to be identified and implemented.

This Chairman's report started with some observations regarding personnel needs in the biomedical sciences. The Foundation's role is to assist the industry—indeed society at large—in meeting those needs. Please understand that the downsizing efforts within the industry were brought about by many factors, not the least of which have been the mergers and acquisitions among the existing members of the industry. Where before there may have been 100 companies, now there may be 60; tomorrow there may be 40.

Of course, the healthcare companies that result from these mergers are larger in terms of personnel, sales and assets than the premerger companies individually. If the Foundation is to successfully pursue its mission, however, newly combined companies need to maintain, if not enhance, their financial support of the Foundation and its programs. Any reduction in support diminishes the Foundation's effectiveness in achieving its core mission of assisting in the development of young scientific researchers and expertise, which helps build alliances within the academic community.

Although I have previously reported to the constituencies of the Foundation as its Treasurer, this is my first PhRMA Foundation Annual Report as Chairman of the Board. My appreciation is extended to former Chairman Charles A. Sanders, M.D., who set a high standard for me to follow. I am also pleased to have the following Board members serving with me during 1995-1996.

#### Mr. G. Gilbert Cloyd

Secretary Treasurer Vice President, Pharmaceuticals Procter & Gamble USA The Procter & Gamble Company

#### Mr. Gordon M. Binder

Chairman and Chief Executive Officer Amgen

#### Mr. Robert A. Ingram

President and Chief Executive Officer Glaxo Wellcome Inc. **Mr. Jan Leschly** Chief Executive SmithKline Beecham plc

**Mr. Sidney A. Taurel** Executive Vice President and President, Pharmaceutical Division Eli Lilly and Company

**Mr. Douglas G. Watson** President Ciba Pharmaceuticals Mr. Robert N. Wilson Vice Chairman, Board of Directors Johnson & Johnson

Mr. Patrick Zenner President and Chief Executive Officer Hoffmann-La Roche Inc.

#### Mr. Gerald J. Mossinghoff President Pharmaceutical Research & Manufacturers of America (Ex-Officio)

My previous terms as Treasurer have provided me with the opportunity to work with Foundation Board President Maurice Q. Bectel and his fine staff, and I am pleased to continue that relationship in my new role as Chairman.

**Robert C. Black** *Chairman, PhRMA Foundation* President Zeneca Pharmaceuticals Group

Celebrating 30 Years

# Report of the President



While Foundation Board Chairman Robert C. Black has addressed some of the underlying changes which have recently taken place in the pharmaceutical industry in his Chairman's Report, I would like to comment on the future funding of the Foundation, then on some new directions.

As the 1994 Treasurer's report (found in this Annual Report) indicates, the basic financial picture of the Foundation continues on sound footing. That achievement has been neither easy nor without casualty, despite the wrenching changes within the industry described by Chairman Black.

Nearly every year since its inception, the Foundation has grown over the previous year—in terms of contributions received, grant applications received and grants awarded. Since 1991, however, the Foundation has been experiencing a decline in contributions received. The continuing trend of mergers and buyouts within the industry continues to reduce the number of eligible contributors, since contributors are limited to active members of the Pharmaceutical Research and Manufacturers of America.

As has been pointed out, when two former contributing companies merge, their subsequent contributions don't always equal the sum of their previous contributions. Of course, we understand that the purpose of the merger was to gain efficiencies in the first place, but that doesn't change the fact that the Foundation's ability to fund and assist developing young biomedical researchers is adversely impacted. As a consequence of reduced contributions, the Foundation's Scientific Advisory Committee and Board were forced to address the hard choices: reduce the number of grants awarded in the existing award categories, consider the elimination of whole categories of grants or both. In actuality, both actions have been taken.

Fewer grants are now awarded in several categories, despite the fact that the need is even greater today, what with the federal cutbacks and reduced NIH funding already adversely impacting biomedical research capacity. Moreover, a \$10,000 grant in 1996 represents a much lesser amount than a \$10,000 grant in 1985, taking inflation into account. Further, the entire category of Faculty Awards in Toxicologic-Pathology has been eliminated, with the Scientific Advisory Committee and the Board concluding that the grants in that subject area had really achieved the Foundation's objectives and, in the face of economic reality, there was but little choice to eliminate this ten-year-old program.

Analyzing some Foundation numbers is also illuminating. Since inception of the Foundation's first awards program, the number of awards categories has been expanded

and now stands at 11. Through 1994, a grand total of 5,260 grant applications had been submitted through the years, with a small minority of only 16% (905) not been approved by the scientifically and intellectually rigorous SAC review process. That means that 84% (4,355) were approved by that same rigorous process, an impressive statistic by any measure.

That's the good news. The not-so-good news is the fact that only 24% (1,225) of the applications were actually awarded the grant monies, due to funding limitations. The remainder (60%; 3,130), were approved but not actually funded. Of even greater concern are the trend lines: as the number of qualified applications continues to rise, unless funding keeps pace, the proportion of those able to be funded is reduced. The need for increased funding is three-fold:

- Inflation eats into the award amounts, which must be increased periodically to keep pace;
- Increased qualified application numbers means that more funds must be available or, alternatively, fewer than the historical 1:4 can actually be awarded; and
- Despite the NIH and other cutbacks, the need for talented biomedical researchers in the research-intensive pharmaceutical industry will continue to grow.

The foregoing is not intended as a lament of the current trends in the industry or the Foundation's affairs; rather it is offered as a rational analysis of the forces at play and the Foundation's reactions and actions for the benefit and understanding of the Foundation's several constituencies. We don't necessarily like all of the circumstances or the decisions we must make, but the Foundation is committed to finding the best balance of what objectives can be achieved with the limited resources available.

In a brighter vein, the Foundation's newest program, the Faculty Development Awards in Pharmacoeconomics, is now up and running, with three grants awarded in 1995 and two more projected for 1996. In a subject area of increasing visibility and interest, the Foundation was advised that the greatest benefit could come from "seeding" the development of teachers and faculty in this relatively new discipline, so that they can go on to teach others the newly-developed and requisite techniques. Also of note, all previous Foundation awards were granted in areas of "hard" science, such as pharmacology or pharmaceutics, whereas pharmacoeconomics is considered differently, in that its researchers deal with data in offices, rather than with patients, animal subjects or chemicals in laboratories.

Also interesting is the mix of initial grant awardees in this new program: two faculty members at schools of medicine and one at a school of pharmacy. We eagerly await their contributions to the body of scientific knowledge in this increasingly important facet of healthcare which assesses both the spectrum of economic cost factors of disease states as well as the quality of life issues so difficult to measure.

So 1995 is a year like no other in the affairs of the Foundation. It is stable and continuing, while at the same time dynamic, challenging and changing. We continue to appreciate the support the Foundation receives from its benefactors, the researchintensive member companies of PhRMA, their representatives who serve as officers and Board members, the many individuals from industry and academe who serve in advisory committee capacities and the more than 2,000 outstanding young scientists and researchers who have been empowered, through Foundation grants, to contribute to biomedical science through their research.

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



### Meetings and Other Activities

#### **TWENTY-FOURTH ANNUAL AWARDEE MEETING**

The PhRMA Foundation Annual Awardee Meeting was held this year on February 8 and 9 at the Washington Vista International Hotel, in Washington, D.C. This meeting provides an excellent forum for the Foundation awardees, the advisory committee members, Board members and staff to learn of the current research being supported by the Foundation as well as the research which has resulted from the support of past awardees.

Over 100 scientists and researchers gathered on Thursday morning, February 9, to observe the Poster Session where awardees-current and former-display their research. The Poster Session was followed by the Annual Awardee Meeting's General Session, at which time the Foundation was pleased to have Michael B. Sporn, M.D., Chief of the Laboratory of Chemoprevention of the National Cancer Institute, as the Thomas E. Hanrahan Memorial Speaker. Dr. Sporn delivered a very current "Pharmacological Overview for Approaches to Cancer Prevention."



Michael B. Sporn, M.D., Chief, Laboratory of Chemoprevention of the National Cancer Institute, delivers the Thomas E. Hanrahan Memorial Lecture. Dr. Renate Reimschussel, 1991 Faculty Awardee in Toxicologic-Pathology, discusses her poster with Hugh Lewis, B.V.M.S., M.R.C.V.S., Dean of the Purdue School of Veterinary Medicine and member of the Pharmacology/Morphology Advisory Committee.



As usual, on the afternoon of February 9, subgroup sessions were held in order for second-year awardees to deliver progress reports on their research and for attendees to hear presentations in their particular disciplines from former awardees and Advisory Committee members.

Presenters at the Clinical Pharmacology Subgroup Session, moderated by Paul Calabresi, M.D., Professor and Chair Emeritus, School of Medicine, Brown University: Jason Umans, M.D., Ph.D., Assistant Professor of Medicine, University of Chicago; Merlin R. Hamre, M.D., Postdoctoral Fellow, Children's Memorial Institute for Education and Research and Northwestern University Medical School; and David W. Rudy, Assistant Professor, Clinical Pharmacology Division, Indiana University.

Presenters at the Basic Pharmacology Subgroup Session, moderated by Irwin Weiner, Dean of the College of Medicine at the State University of New York, HSC, Brooklyn: Mark Leid, Ph.D., Assistant Professor of Pharmacology, College of Pharmacy, Oregon State University; Elias Lolis, Ph.D., Assistant Professor of Pharmacology, School of Medicine, Yale University; and Bih-Hwa Shieh, Ph.D., Assistant Professor of Pharmacology, School of Medicine, Vanderbilt University.

Presenters at the Pharmacology/Morphology Subgroup Session, moderated by Michael D. Gershon, M.D., Professor and Chairman of the Department of Anatomy and Cell Biology at Columbia University, College of Physicians and Surgeons: Holly Boettger-Tong, Ph.D., Postdoctoral Fellow in Pharmacology, University of Texas, Health Science Center, Houston; Song Song, M.D., Postdoctoral Fellow at Harvard University Medical School; and Dorie W. Schwertz, Ph.D., Associate Professor, Department of Pharmacology and Medical Surgical Nursing, of the College of Medicine and College of Nursing, University of Illinois, Chicago.

For the first time in 1995, Pharmaceutics awardees gave presentations at the Pharmaceutics Subgroup Session, moderated by Lynda M. Sanders, Ph.D., formerly with Syntex Laboratories: Hartmut C. Derendorf, Ph.D., Professor and Chairman, College of Pharmacy, University of Florida; Prashant J. Chikhale, Ph.D., Assistant Professor in Pharmaceutics and Biotechnology at the School of Pharmacy, University of Maryland, Baltimore; and Philip C. Smith, Ph.D., Assistant Professor, Division of Pharmaceutics, School of Pharmacy, University of North Carolina, Chapel Hill.



Honored at the PhRMA Foundation Annual Awardee Banquet on February 8, C. Joseph Stetler, Esq., applauds the Foundation and encourages PhRMA member companies to step up their support of the Foundation's vital work. Mr. Stetler, former President of PhRMA and the Foundation, retired as Counsel to the Foundation in June 1994.

C. Joseph Stetler, Esq., retiring as Counsel to the PhRMA Foundation, was honored at the Annual Awardee Banquet, the evening of February 8. Mr. Stetler has the distinction of serving as President of the Foundation for over 13 years, during his tenure as President of the then-Pharmaceutical Manufacturers Association. In his after-dinner remarks, Mr. Stetler recounted the Foundation's track record in building the careers of many of those present. He further defined the importance of the Foundation's role in the academic community during the past 30 years of the Foundation's rich history, at which time he challenged the pharmaceutical research-intensive members of PhRMA to increase their support of the Foundation which has jump-started the careers of these bright, young scientists. Maurice Q. Bectel, PhRMA Foundation President, on behalf of the Board, Advisory Committee members, staff and awardees, presented Mr. Stetler with a crystal mortar and pestle for his dedication and wise counsel over the years.

# PHRMA FOUNDATION BOARD OF DIRECTORS SPRING MEETING, WASHINGTON, D.C.

At its March 26, 1995, meeting, this year held at the Mayflower Hotel in Washington, D.C., the PhRMA Foundation Board of Directors elected new officers: Mr. Robert C. Black, President, Zeneca Pharmaceuticals Group, as Chairman; and, Mr. G. Gilbert Cloyd, Vice President, Pharmaceuticals, Procter & Gamble USA, Procter & Gamble Company, as Secretary-Treasurer. Philip R. Tracy, Chief Executive Officer and President of Burroughs Wellcome Co., turned the gavel over to Mr. Black, after filling the unexpired term of Charles A. Sanders, M.D., then-Chairman of Glaxo Inc., who retired from the Foundation Board in December 1994. The position of Vice Chairman was temporarily left open due to the restructuring of PhRMA Foundation Board member companies. The PhRMA Foundation Board welcomed two new members during the past year—Mr. Robert A. Ingram, President and Chief Executive Officer, Glaxo-Wellcome Inc., and Douglas G. Watson, President, Ciba Pharmaceuticals.

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 Black, Cloyd, Ingram and Watson, Board members serving are: Mr. Gordon M. Binder, Chairman and Chief Executive Officer, Amgen; Mr. Jan Leschly, Chief Executive, SmithKline Beecham plc; 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; and, Mr. Patrick J. Zenner, President and Chief Executive Officer, Hoffmann-La Roche Inc.

The Spring Meeting of the PhRMA Foundation Board of Directors is held every year in conjunction with the PhRMA Annual Meeting.

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# Education and Training Programs

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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 12 funding programs—four in clinical pharmacology, two in pharmacology/toxicology, one in the combined field of pharmacology-morphology, three in pharmaceutics and one in pharmacocommics (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 at three levels-students, postdocs and faculty.

#### FACULTY AWARDS IN CLINICAL PHARMACOLOGY

The Foundation Faculty Development Awards in Clinical Pharmacology program makes three-year awards to medical schools for salary and fringe benefits support of full-time junior faculty members. A ceiling of \$40,000 has been set on the amount of Foundation participation in total yearly salary and fringe benefits for any candidate.

With the awards beginning July 1, 1994, 104 individuals have been supported under this program since 1967.

#### Recipients of the awards which began July 1995 are:

James Francis Cleary, M.B., B.S., F.R.A.C.P., Research Associate/ Clinical Instructor, Department of Human Oncology, University of Wisconsin - Madison, School of Medicine: "Therapeutics in the Treatment of Cancer Patients." The goal of cancer treatment can either be palliation or cure. Morphine, the mainstay of cancer pain palliation, is metabolized to morphine-6-glucuronide (M-6-G), morphine 3-glucuronide and normorphine. M-6-G is a more potent analgesic than morphine and is likely to be important in the analgesia



of morphine. However, a dose-effect relationship for morphine and its metabolites has not been defined. In this study, cancer patients with severe pain (pain score  $\geq$  7) will be treated with morphine to a pain level of  $\leq$  4 (mild pain) and the concentration of morphine and its metabolites measured in urine and plasma. The pharmacokinetics of morphine and its metabolites will be correlated with the analgesic and the side effects of the morphine dose administered. The effect of age and race on the dose-effect relationship will be studied. Incubation of morphine with hepatic microsomes will allow the effect of age, liver disease and co-administered drugs on the formation of morphine metabolites to be documented. The pharmacokinetics and analgesia of the conversion from intravenous to oral morphine will be examined and the relative potency of the two formulations compared. The cure of cancer remains an important goal and phase 1 studies of new anti-cancer drugs, the initial step in the development of new treatments, will be concluded.



Lionel David Lewis, M.B. Chir., M.R.C.P., M.D., Assistant Professor, Division of Clinical Pharmacology, Dartmouth Medical School: Project 1: "The relationship between mitochondrial DNA replication and the pancreatic toxicity of anti-HIV nucleoside analogs." The primary hypothesis is that the 2'3'-dideoxynucleoside triphosphates formed intracellularly from ddI (and ddC) inhibit mitochondrial DNA polymerase gamma leading to pancreatic cytotoxicity. Pancreatic tumor cells will be incubated with differing concentrations of ddI (and ddC) in order to investigate: (1) the effects of ddI (and ddC) on

mitochondrial biogenesis, structure and function; (2) the global intracellular and mitochondrial metabolism of ddI (and ddC); and, (3) the potential of antioxidants (e.g. alpha-tocopherol) to ameliorate pancreatic toxicity of ddI (and ddC) *in vitro*.

Project 2: "A Phase-1 study of combination therapy with paclitaxel (Taxol) and fractionated ifosfamide in patients with stage IV or recurrent lung cancer." The study objectives are: (1) to define the maximal tolerated dose of paclitaxel/fractionated ifosfamide; (2) to investigate the pharmacokinetics of each drug when combined, and to discover whether there is a sequence effect; and, (3) to investigate the effect of the combined paclitaxel/fractionated ifosfamide chemotherapy on CYP450IIIA metabolic activity. Each dose cohort in this escalating-dose protocol will undergo a balanced randomization to receive either treatment A (Paclitaxel preceding fractionated ifosfamide) or treatment B (fractionated ifosfamide preceding paclitaxel) on the first treatment occasion. Each dose cohort will then receive the alternate treatment 28 days later. Appropriate blood and urine samples will be obtained in order to determine the pharmacokinetics of each drug. In addition, the effects of each drug upon the activity of CYP450IIIA will be determined.



**Charles Michael Stein, M.B.Ch.B., M.R.C.P.,** Assistant Professor, Division of Clinical Pharmacology, Vanderbilt University School of Medicine: "Ethnicity and Vascular Reactivity." Hypertension is a major problem in African-Americans and ethnic differences in the regulation of vascular tone may be important in the pathogenesis of hypertension. Evidence for such ethnic differences includes increased responsiveness to stress and increased salt sensitivity in blacks. Altered vascular responsiveness and/or increased sympathetic activity have been suggested as possible explanations for this increased

pressor response but the methods used to investigate these mechanisms have been inadequate. We have examined the regulation of vascular tone in African-Americans using methods that allow accurate determination of both sympathetic activation and vascular response without the confounding variable of activation of systemic reflexes. Initial studies show that forearm blood flow responses to isoproterenol are markedly blunted in Mrs. Sally Bambach, wife of former PMA General Counsel Karl Bambach, Ph.D., Barbara Hanrahan, wife of former Foundation President Tom Hanrahan, and Mrs. Norine Stetler, wife of Joe Stetler, enjoy a few moments discussing "old times" before the Annual Awardee Banquet.



normotensive African-Americans, suggesting an important ethnic difference in the regulation of vascular tone. Building on our experience in the areas of vascular tone regulation and inter-ethnic differences in drug response, we propose to further characterize the attenuated response to  $\beta$ receptor agonists observed in African-Americans and identify potential ethnic differences in the regulation of vascular response and sympathetic activity. The regulation of sympathetic activity, both systemically and locally in the forearm, and the relationship between sympathetic activity and vascular response to agonists infused directly into the brachial artery will be determined. These studies will allow us to determine if interethnic differences in the regulation of vascular tone exist and will contribute significantly to our understanding of hypertension generally and hypertension in blacks specifically.

#### Recipients of the award 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."

**Richard B. Kim, M.D.,** Assistant Professor, Division of Clinical Pharmacology, Vanderbilt 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."

**Andre Terzic, M.D.,** Assistant Professor of Medicine and Pharmacology, Mayo Clinic, Mayo Medical School (Mayo Foundation): "Molecular Pharmacology of Cardiotonic and Cardioprotective Regulation."

#### Those who began their awards in 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 began their awards in 1992 and end their awards in 1995 are:

Joshua Olajide Atiba, M.B., Assistant Professor of Medicine and Pharmacology, University of California, Irvine (actually began his second year in 1993).

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.

#### FELLOWSHIPS FOR CAREERS IN CLINICAL PHARMACOLOGY

The second program in clinical pharmacology provides "Fellowships for Careers in Clinical Pharmacology"-a postdoctoral award. 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 1995 may request that the fellowship begin July 1996 or July 1997.

First awards under this program were made in 1973. Since that time, 61 fellowships have been awarded.

#### Recipients of the award beginning July 1, 1995:



**Sara Browne, M.D.,** Division of Clinical Pharmacology, Stanford University Medical Center: "Temporal Regulation of Ca2+/Calmodulin Dependent Protein Kinase (CaM kinase) by Intracellular Ca2+ Oscillations." The multifunctional enzyme Ca2+/Calmodulin dependent protein kinase (CaM kinase) is a major mediator of Ca2+ linked signal transduction systems. This enzyme phosphorylates diverse substrates in response to extracellular signals which elevate intracellular Ca2+. Given the enzymes' broad substrate specificity and the ubiquity of Ca2+ as an intracellular second messenger, how can

specificity of hormone response be achieved? The recently discovered biochemical properties of CaM kinase and theoretical models of CaM kinase activity have led to the hypothesis that CaM kinase functions as a molecular device that decodes the frequency of intracellular Ca2+ oscillations, i.e. a type of temporal regulation, which allows the cell to achieve response specificity to hormone or neurotransmitter stimulation. As a corollary of this, Dr. Schulman has proposed that different subunit compositions within CaM kinase holoenzyme will affect the decoding properties of the enzyme. To test this hypothesis, I will study how the frequency of Ca2+ oscillations affects the activity and autophosphorylation of CaM kinase both *in vitro* and *in situ*. The *in vitro* approach will consist of using immobilized kinase (developed in Schulman's lab) and exposing it to various frequencies of delivered calcium. The *in situ* approach will involve studying CaM kinase autophosphorylation and its activation of a specific substrate, a C1-channel providing a physiological read out of enzyme activity in response to Ca2+ oscillations. The latter will

be achieved using patch-clamp physiology. The pathway to be studied utilizes a chloride channel distinct from the one defective in cystic fibrosis (CF) and thus holds therapeutic potential for circumventing defective regulation of C1 channels in CF.

**Patrick Thomas Murray, M.D.**, Section of Nephrology, Pritzker School of Medicine, University of Chicago: "Mechanism of Endotoxininduced Vascular Dysfunction." This research aims to determine: (1) whether the endothelial and smooth muscle changes induced by endotoxin (bacterial lipopolysaccharide, LPS) in conduit vessels also occur in systemic resistance-caliber vessels (producing the characteristic hemodynamic profile of sepsis); and (2) the mechanism whereby vascular smooth muscle contraction is impaired. Preliminary studies suggest that LPS exposure impairs vascular contraction



principally by inducing the abnormal synthesis of NO by inducible NO synthase (iNOS), and also inhibits vasorelaxant-stimulated EDRF synthesis by interfering with the activity of endothelial NO synthase (eNOS). Studies will be performed assessing contractile and vasorelaxant function in isolated microvessels and vascular beds, and using vessel permeabilization and spectrofluorimetry (with fura-2, on cultured cells) to dissect the mechanism of the contractile defect. Definition of these phenomena should facilitate titration of hemodynamic support for septic patients, thus decreasing morbidity and mortality from refractory hypotension and progressive multiple organ failure.

#### Recipients of the award beginning July 1, 1994:

**Richard Z. Lin, M.D., M.P.H.,** Stanford University School of Medicine, Harvard Medical School, Harvard University: "A Mechanism of á Adrenergic Receptor Desensitization; Endothelium-Derived Relaxing Factor."

**Merit Cudkowicz, M.D.,** Harvard Medical School, Harvard University: "Therapeutic Trial of Free Radical Scavengers in Amyotrophic Lateral Sclerosis."

Raymond W. Urbanski, M.D., Ph.D., Jefferson Medical College, Thomas Jefferson University: "Targeted Cytotoxicity of Colorectal Tumors by E. Coli ST."

Beginning his award in July of 1993 and ending his award in 1995:

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

Explaining a few points from his research poster, Dr. Jeffrey A. Hughes, University of Florida, displays his research originally supported by the PhRMA Foundation through a Postdoctoral Fellowship in Pharmaceutics at the University of North Carolina, Chapel Hill. Margaret Dordal, Ph.D. (on left) received a 1992 Faculty Development in Pharmacology at Northwestern University Medical School.





Former awardee and long-time friend of the Foundation, I.K. Ho, Ph.D., Professor and Chairman of the Department of Pharmacology, University of Mississippi Medical Center, and Rochelle Schwartz, Ph.D., 1987 Faculty Development Awardee in Pharmacology, spend time viewing the 30 posters at the Annual Awardee Meeting Poster Session on February 9, 1995.

#### 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. Onehundred seventeen awards have been made since 1974.

#### Individuals whose awards began in July 1995 are:

**Joshua Garren**, Brown University, School of Medicine: "A Model for Studying Activity-Dependent Synaptic Development" (One-year Award). Mr. Garren's fellowship supervisor is Mark Bear, Professor of Neuroscience.

**Margaret McKernan**, University of Texas Medical Branch: "The Amygdala AMPA Receptor: Role in Fear Conditioning" (One-year Award). Ms. McKernan's fellowship supervisor is Patricia Shinnick-Gallagher, Ph.D., Professor of Pharmacology.

**Jason E. Reynolds**, Dartmouth Medical School: "Role of MAP Kinase in Regulating Apoptosis" (One-year Award). Mr. Reynolds' fellowship supervisor is Dr. Alan Eastman, Professor, Department of Pharmacology/Toxicology.

**Jonathan Lawrence Schreiber**, Duke University, School of Medicine: "Characterization of the Interactions Responsible for the Activation of Calcium/Calmodulin-Dependent Protein Kinases" (One-year Award). Mr. Schreiber's fellowship advisor is Anthony R. Means, Ph.D., Chairman, Department of Pharmacology.

### **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 64.

#### Recipients of the 1995 Faculty Development Awards in Pharmacology are:

**Emery H. Bresnick, Ph.D.**, Assistant Professor, Department of Pharmacology, University of Wisconsin-Madison, Medical School: "Mechanism of the Human  $\beta$ –Globin Locus Control Region." The human  $\alpha$ - and  $\beta$ -globin polypeptides combine to form the hemoglobin tetramer that is essential for distributing oxygen throughout the body. The restriction of globin synthesis to cells of the erythroid lineage represents a fundamental problem in molecular hematology. The transcriptional activity of the  $\beta$ -globin genes is controlled by four erythroid-specific DNaseI hypersensitive sites (hss) at the 5'-end of the

globin locus. This locus control region (lcr) is crucial for maintaining the globin cluster in an "active" chromatin conformation. The goal of this project is to understand how the components of the lcr interact to establish an autonomously regulated chromosomal domain during erythropoiesis. Dr. Bresnick's research will discriminate between two inclusive models for the mechanism of the lcr, in which the hss function independently or as an integrated unit. The laboratory will use biochemical and molecular biological approaches to test their hypothesis that the hypersensitive cores represent ordered complexes. Elucidating the molecular mechanism of the lcr has important practical implications for expressing genes in transgenic organisms and human gene therapy. Moreover, understanding how the lcr functions will facilitate the design of synthetic lcrs that are more efficacious than natural ones and could lead to new therapeutic approaches for hematologic disorders such as sickle cell anemia and thallasemias.

**Haian Fu, Ph.D.,** Assistant Professor, Department of Pharmacology, Emory University, School of Medicine: "Role of 14-3-3 Proteins in Cellular Signal Transduction." Identification of key components of cellular pathways directly responsible for human disease has led to the development of a new generation of highly specific, small molecule drugs for the treatment. Dr. Fu's research focuses on a family of growth controlling molecules, the 14-3-3 proteins, thus may provide novel strategies for the development of anti-cancer drugs. 14-3-3 proteins are highly conserved, ubiquitous eukaryotic molecules.

They are involved in controlling cell division, and have been found to associate with the protein products of both a viral oncogene (MT) and cellular proto-oncogenes (*raf* and *bcrabl*), likely contributing to human disease processes. This research will specifically focus on the interaction of 14-30-3 proteins with *Raf*-1, a central component of multiple signal transduction pathways, which functions in the control of cell growth, transformation and differentiation. The initial emphasis of this research will be to delineate the *Raf*-binding site of 14-3-3 and to test the functional consequence of the 14-3-3 interaction on *Raf* 





action. To provide a structural basis for 14-3-3 interaction, 3-dimensional structure of 14-3-3 $\zeta$  will be determined. These studies should contribute to our basic understanding of cell growth regulation and oncogenesis. The detailed information the molecular recognition events at the interface of 14-3-3 and *Raf* may provide structure-based approaches for developing novel anti-cancer drugs which specifically target at the *Raf* step of the signal transduction pathways; for example, for the purpose of blocking the P21<sup>ras</sup>mediated malignancy.

Those entering their second year in 1995 are:

James E. Ferrell, Jr., M.D., Ph.D., Stanford University, School of Medicine: "The Link from *Ras* to *Raf-1*."

**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."

**Brian E. Wadzinski, Ph.D.,** Vanderbilt University, School of Medicine: "Localization and Targeting of Protein Ser/Thr Phosphatases in Mammalian Cells."

Individuals who ended their awards in 1995:

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.

#### 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.



Edward J. Cafruny, M.D., Ph.D., Foundation Scientific Consultant, Distinguished University Professor and Former Dean of the Undergraduate School of Biomedical Sciences at the University of Medicine and Dentistry of New Jersey, moderates the General Session of the Annual Awardee Meeting, February 9, 1995. Mr. C. Joseph Stetler and Dr. E. Leong Way, University of California, San Francisco, reminisce over the Foundation's vital work during the last 30 years. Mr. Stetler served as the Foundation President in his capacity as President of the Association from 1965 until 1978 and Eddie Way has served on the Basic Pharmacology Advisory Committee since 1973 and on the Scientific Advisory Committee from 1973 until 1993.



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 18th year, has awarded a total of 219 fellowships.

# Those who have been awarded 1995 fellowships beginning between January through July are:

**Abdul Hafeez Diwan**, University of South Alabama, College of Medicine: "Mechanism(s) of Regulation of Rat Pulmonary Microvascular Endothelial Cell Permeability by Cyclic GMP" (18 months). Disturbance of microvascular endothelial permeability contributes to fluid accumulation (edema) in pulmonary diseases (e.g. bronchitis). The aim of this research is to define the molecular and intracellular mechanisms that govern this function. The studies proposed should help toward designing appropriate drug therapy to treat pulmonary disorders in the future. Thesis Advisor: Samuel J. Strada, Ph.D., Professor and Chairman, Department of Pharmacology.

**Qian Li**, Loyola University, Stritch School of Medicine: "Biochemical and Functional Changes in 5-HT1A Receptors During Exposure to 5-HT Reuptake Inhibitors." This project will characterize the adaptional changes in the density and affinity of 5-HT<sub>1A</sub>, receptors, their G protein coupling and their functions during the first three weeks of exposure to 5-HT uptake inhibitors, fluoxetine and paroxetine. The function of 5-HT<sub>1A</sub> receptor systems will be evaluated from hormone responses to 5-HT<sub>1A</sub> agonists. Thesis Advisor: Dr. Louis D. Vann de Kar, Professor, Department of Pharmacology.

**Asli Memisoglu**, Harvard University, School of Public Health: "Cloning and Characterization of *S.Pombe* cINAs that Provide Resistance to Alkylating Agents." Alkylating agents are an abundant class of toxicants. Using the fission yeast *Schizosaccharomyces pombe* as a model, five genes have been identified that provide resistance to the lethal effects of alkylation damage. Future studies are aimed at elucidating the mechanisms by which these gene products provide alkylation resistance. Thesis Advisor: Leona Samson, Ph.D., Professor, Department of Molecular and Cellular Toxicology. **Shira Rohde**, Columbia University, Graduate School of Arts and Sciences: "Alpha<sub>1</sub>-Adrenergic Receptor Subtype Activation of Protein Kinase C Isoforms in the Heart." Catecholamines modulate cardiac contractile performance and induce features of the hypertrophic phenotype via actions at  $\alpha_1$ -adrenergic receptors. This research is designed to implicate specific  $\alpha_1$ -adrenergic receptor subtypes and isoforms of PKC in these catecholamine actions. This information ultimately should provide novel strategies to selectively inhibit the deleterious actions of catecholamines in the setting of cardiac failure. Thesis Advisor: Dr. Susan Steinberg, Associate Professor of Medicine and Pharmacology.

**W. Daniel Stamer**, University of Arizona, College of Medicine: "Functional Relationship Between Alpha<sub>2</sub> Adrenergic Receptors and AQP-CHIP" (18 months). Alpha<sub>2</sub> Adrenergic Receptors and CHIP water channels are known to be present in tissues that are involved in the directional movement of water, such as in the non-pigmented ciliary epithelium of the eye and the proximal tubules of the kidney. The goal of this project is to investigate a possible functional relationship between receptor activation and CHIP-mediated water transport. Thesis Advisor: John W. Regan, Ph.D., Associate Professor of Pharmacology-Toxicology.

**Zhuangqun (Galen) Wo**, Cornell University, College of Veterinary Medicine: "Structural and Functional Characterization of Inotropic Glutamate Receptors." The primary excitatory neurotransmitter receptors in vertebrate brain are proteins which bind glutamate and allow ions to enter cells. This laboratory has cloned two glutamate receptors from goldfish brain. Work on these proteins has and is continuing to yield important insight into glutamate receptor structure. Thesis Advisor: Robert E. Oswald, Ph.D., Professor, Department of Pharmacology.

**Shelly Demeris Wood**, Emory University, School of Medicine: "Interactions Between Coexisting Beta Adrenergic Receptor Subtypes in Cell Signaling." Multiple receptor subtypes mediate the responses to adrenaline and can coexist in tissues or single cells. The functional roles and relative importance of each subtype is unclear. This study will investigate how closely related subtypes interact to determine the cellular response and the importance of the density and ratio of each subtype present. Thesis Advisor: Kenneth P. Minneman, Ph.D., Professor, Department of Pharmacology.

**Chen Yan,** University of Washington, School of Medicine: "Differential Distribution and Physiological Function of Multiple Splicing Variants Encoded by a Novel Calmodulin-Dependent Phosphodiesterase Gene." The specific aims of this project are: (1) to express and characterize biologically active PDE]C; (2) to determine the differential, regional and cellular expression of distinct PDE]C mRNAs; (3) to use pharmacological approaches to examine two possible functions of PDE]C isozymeds in Ca<sup>2+</sup> mediated regulation of intracellular cyclic nucleotide levels in cerebellar granule cells and olfactory neurons. Thesis Advisor: Joseph A. Beavo, Ph.D., Professor, Department of Pharmacology.

**Run Yu**, University of Rochester, School of Medicine and Dentistry: "Mechanisms and Functions of Endocytosis of the Thyrotropin-Releasing Hormone Receptor." This study will investigate the molecular basis of specific interactions between G proteins and their effectors. Results from this study will not only give insights into how G proteins interact with effectors, but also provide potential targets for developing drugs that enhance and attenuate the biological processes mediated by these signal transduction pathways. Thesis Advisor: Patricia M. Hinkle, Ph.D., Professor of Oncology in Pharmacology.



William A. Darrow, M.D., Chairman of the Scientific Advisory Committee and Senior Medical Advisor for the Schering-Plough Research Institute, addresses the attendees at the Annual Awardee Meeting Luncheon on February 9.

**Kehong Zhang**, Louisiana State University, Medical Center: "Involvement of Beta Adrenergic Receptors in the Behavioral Effects of Antidepressants." Central betaadrenergic receptors are involved in the actions of antidepressant drugs as evidenced by the receptor density change following chronic administration and the behavioral effects of the receptor ligands. This study will further characterize the role of central betaadrenergic receptors in the behavioral effects of antidepressants with antisenses that block the receptor expression. Thesis Advisor: James M. O'Donnell, Ph.D., Associate Professor of Pharmacology and Therapeutics.

### 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, 94 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 1995 are:



**Hui Pan, M.D.,** Columbia University, College of Physicians and Surgeons: "Signal Transduction in Serotonergic Neurons in the Peristaltic Reflex Pathway." This project is designed to provide training in modern techniques in morphological research that will complement training that Dr. Pan has already received in pharmacology. The enteric nervous system (ENS) is the only region of the PNS that is able to manifest reflex activity in the absence of input from the brain or spinal cord. This capability is made possible by intrinsic reflex pathways, which include primary afferent neurons and

interneurons, in the wall of the bowel. One such reflex is the peristaltic reflex. Previous observations have suggested that 5-HT plays a critical role in the peristaltic reflex pathway and that its critical actions are mediated by a novel receptor subtype,  $5=T_{IP}$ , which has, until now only been characterized operationally (pharmacologically). Dr. Pan then proposes to define the signal transduction pathway responsible for 5-HT<sub>IP</sub>-mediated responses. He will test the hypotheses that 5-HT<sub>IP</sub> receptor is coupled to Go, that the pathway involves activation of one or more isoforms of protein kinase C(PKC). He will then test the idea that PKC activates type 2 adenyl cyclase, to increase cAMP and activate protein kinase A, which amplifies the response. Finally, he will employ a genetically engineered mutant pseudorabie virus to identify all the cells of the entire peristaltic reflex microcircuit. This study will test the prediction that serotonergic interneurons are components of that pathway. The research will utilize, in addition to electrophysiology, morphological methods, including immunocytochemistry, *in situ* hybridization, image processing and retrograde tracing of neural pathways with a viral probe.



**Christine Saunders, Ph.D.**, School of Medicine, Vanderbilt University: "Adrenergic Receptor Involved in Targeting/Retention to the Basolateral Domain of Polarity Epithelial." The goal of this research is to elucidate the structural features of the Alpha<sub>2A</sub>adrenergic renal epithelial cells. Since Alpha<sub>2A</sub>-AR localization in specialized subdomains of target cells provides an important first step in determining which G-proteins and effectors these receptors can interact with, understanding the mechanisms by which this specialized localization occurs is a first step in suggesting novel

therapeutic strategies either to foster or disrupt G-protein coupled receptor targeting in particular disease states, as what is learned for the Alpha<sub>2A</sub>-AR should be applicable to other G-protein-coupled receptors. Observations in this laboratory indicate that the Alpha<sub>2A</sub>-AR is directly targeted to the basolateral surface of Madin-Darby canine kidney (MDCKII) cells, a renal epithelia polarized model system that accurately reflects Alpha<sub>2A</sub>-AR localization *in vivo*. Mutagenesis studies of the Alpha<sub>2A</sub>-AR suggest that domains in the bilayer of this seven transmembrane-spanning receptor confer targeting whereas endofacial domains facilitate retention on the basolateral surface. In contrast, recent data indicate that the A1 adenosine receptor trafficks apically in MDCKII cells. Thus, chimeras of Alpha<sub>2A</sub>-AR and A1 receptors should reveal which bilayer regions contribute to basolateral vs. apical targeting. The cellular fate of the chimeric structures will be examined both biochemically and morphologically, using laser scanning confocal microscopy and immunodetection to determine steady stae polarization and timedependent appearance of Alpha<sub>2A</sub>-AR, A1 receptors and receptor chimeras at their ultimate location.



Dr. Michael Sporn (L) elaborates on his presentation with Dr. Edward J. Cafruny, Foundation Scientific Consultant, and Dr. Irwin Weiner, Chairman of the Foundation's Basic Pharmacology Advisory Committee and Dean of the SUNY School of Medicine, Brooklyn.

Individuals who entered the second year of their awards in 1995 are:

Min-Tsai Liu, D.D.S., Columbia University, College of Physicians and Surgeons: "Characteristics of Pancreatic Neurons and Their Response to 5-HT."

**Sally Schroeter, Ph.D.,** Emory University, School of Medicine: "Ontogeny of the Antidepressant-sensitive 5HT Transporter." Dr. Schroeter transferred her award to Vanderbilt University School of Medicine in early 1995.

Individuals who ended their awards in 1995 are:

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

Miles Orchinik, Ph.D., Rockfeller University.

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

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

### 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 at a school of pharmacy-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.

The pharmaceutics faculty member applies for the award and, once selected, is provided with a one-year, \$5,000 fellowship which the faculty member can provide to a qualified undergraduate of his or her choosing. Nine awards were made for 1995, bringing the total number of awards to 67.

Faculty and their undergraduate students who received fellowships between January and August 1995 are:

Janet P.F. Bai, Ph.D., Assistant Professor, Pharmaceutics Department, College of Pharmacy, University of Minnesota.

**Student: Hae Jin Hong**, "Intestinal Absorption of Etoposide"—This research includes the fundamental aspects of delivery of biotechnology products and absorption of chemotherapeutic agents.

Kenneth A. Connors, Ph.D., Professor, School of Pharmacy, University of Wisconsin-Madison.

**Student: Rachel V. Leiterman**, "Solvent Effects on the Stability of  $\alpha$ -Cyclodextrin Complexes of 4-Nitrophenol and 4-Nitrophenolate"—The stabilities of "host-quest" inclusion complexes of 4-nitrophenol and of 4-nitrophenolate in the macrocyclic host  $\alpha$ -cyclodextrin will be studied in binaryaquenous-organic solvent mixtures to learn the energetic sources of these complexes' stabilities.

James N. Herron, Ph.D., Associate Professor, Department of Pharmaceutics, School of Pharmacy, University of Utah.

**Student: Brian Buffington**, "Recombinant Antibodies as Targeting Moieties in Immunoliposomes"—The goal of this project is to refine the antibodies used in immunoliposomes, a specialized drug delivery system, so that they become more effective targeting moieties. Presently, the choice of antibodies that can be coupled to liposomes is somewhat limited by formulation issues.

Jeffrey Hughes, Ph.D., Assistant Professor, Department of Pharmaceutics, College of Pharmacy, University of Florida.

**Student: Pam Mitchell**, "Development of a Fluorescence Technique to Study Oligonucleotide Stability"–Biotechnology derived products such as oligonucleotides (ODN) stability studies are problematic due to the numerous reactions which can occur. This study will develop fluorescence-based techniques to study the ODN degradation pathways. This information will be used to develop better formulations of ODN.

Vincent H. L. Lee, Ph.D., Professor and Chairman, Department of Pharmaceutical Sciences, School of Pharmacy, University of Southern California. Student: Lan Ngoc Nguyen, "Antiviral Drug Transport Across Infected Tracheal Epithelial Cell Monolayers"—This research seeks to determine how viral infection will affect the permeability of lung cells to drugs.

**Curtis T. Okamoto, Ph.D.,** Assistant Professor, Department of Pharmaceutical Sciences, School of Pharmacy, University of Southern California.

**Student: Hagop Hajian**, "Transcytosis of Intrinsic Factor by Intestinal Epithelial Cells"– This research proposes to characterize the physiologically relevant apical-to-basal transcytosis of intrinsic factor-cobalamin complexes by the intrinsic factor receptor in cultured intestinal epithelial cell lines.



Sharing a moment at the reception on February 8 are (L to R) Russell A. Bantham, PhRMA Senior Vice President and General Counsel, Dr. Art Hayes, and Dr. John F. Beary III, PhRMA Senior Vice President of Science and Regulatory Affairs **Nita K. Pandit, Ph.D.,** Associate Professor, College of Pharmacy and Health Science, Drake University.

**Student: Jayesh Kanjia**, "Effect of Additives on the Repulsive Interaction Between Nonionic Surfactants and Polyethylene Glycol in Aqueous Solution"—Interactions between polymers and surfactants in pharmaceutical products can dramatically affect the properties of these materials. This research project will examine the interaction between polyethylene glycols and selected non-ionic surfactants, and determine how the interaction affects the water solubility of these materials.

**Dennis H. Robinson, Ph.D.,** Associate Professor, Department of Sciences, College of Pharmacy, University of Nebraska Medical Center.

**Student: Barbara Keuter**, "Synthesis and Characterization of Carbamate Derivatives of Deferoxamine"–Deferoxamine, the drug used to treat iron poisoning, must be injected as it is relatively ineffective when swallowed. This project aims to synthesize new derivatives of deferoxamine with properties that enable patients to take the drug orally.

**Philip C. Smith, Ph.D.,** Assistant Professor, Division of Pharmaceutics, School of Pharmacy, University of North Carolina at Chapel Hill.

**Student: Mohammad Banawan**, "Studies of the Reactivity and Pharmacokinetics of Acyl Glucuronide Metabolites of Phenyl Glycines in the Rat"—A series of phenyl glycine analogs have been identified to cause hepatobiliary toxicity in rats. This research will investigate the correlation between their metabolism to reactive acyl glucuronides, biliary exposure and covalent protein binding in the rat.

## 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. Five awards were made for 1995 bringing the total number of awards made to 51.

#### Those who received fellowships beginning between January and July 1995 are:

**Nicholas P. Chetwyn**, School of Pharmacy, University of Kansas: "Development of Techniques for Rapidly Screening Biological Activity-Enzyme Based Biosensors for Capillary Electrophoresis with Electrochemical Detection." The ability to detect and rapidly screen compounds for biological activity is becoming increasingly more important. The objective of this research is to design and develop a system which couples highly efficient capillary electrophoretic separation with an on-line enzyme based bio-sensor. The bio-sensor takes advantage of the high sensitivity of electrochemical detection to detect biologically active species in the model system. Thesis Advisor: Christopher M. Riley, Ph.D., Professor of Pharmaceutical Chemistry. **Mark Douglas Johnson**, School of Pharmacy, University of Utah: "Enzyme-Based Approaches Toward Understanding and Optimizing the Central Nervous System (CNS) Delivery Potential of Anti-HIV Nucleoside Derivatives." Many of the nucleoside derivatives effective in the treatment of systemic infections (i.e. 2', 3'-dideoxyinosine) are quite polar and therefore exhibit limited penetration into the central nervous system (CNS). Recent studies of the uptake kinetics of several dideoxynucleoside into the CNS yielded exceptionally low apparent rate constants for entry and unexpectedly large apparent rate constants for efflux. Through both *in vitro* and *in vivo* experiments with existing dideoxynucleosides and newly synthesized enzyme activated prodrugs, the contributions of both transport and metabolism to the uptake and efflux kinetics will be defined. Thesis Advisor: Bradley D. Anderson, Ph.D., Professor, Pharmaceutics and Pharmaceutical Chemistry.

**Roderike Pohl**, School of Pharmacy, University of Connecticut: "Determination of Transepithelial Pathways Underlying the Alveolar Absorption of Macromolecules." Alveolar regions of the lung offer considerable promise as sites for the absorption of therapeutic macromolecules, but mechanisms underlying such absorption are unknown. These studies will use fluorescence scanning confocal and electron microscopes to identify important pathways with the ultimate objective of optimizing physical-chemical and formulation characteristics of macromolecules delivered via this route. Thesis Advisor: Paul A. Kramer, Ph.D., Professor of Pharmaceutics.

**Negar Sadrzadeh**, School of Pharmacy, University of Wisconsin, Madison: "Interfacial Properties in Mixtures of Lipids and Polymers." Mixtures of small and large amphophilic substances are of fundamental importance because of their role at interfaces in affecting the properties of such diverse systems as biological membranes and pharmaceutical dispersions. This research will use model lipid-polymer mixtures to probe both the mixing tendencies in such systems as well as the effect of the polymer on the fluidity of the lipid layer. Thesis Advisor: George Zografi, Ph.D., Professor of Pharmaceutics.

**Minli Xie**, School of Pharmacy, University of Kansas: "Hot Spots in Degradation of Protein and Peptide Drugs." Asparagine deamidation and aspartate transmidation are two major degradation pathways of protein and peptide drugs which lead to reduced activity and integrity of pharmaceutics. Both reactions involve the same reaction intermediate, a cyclic imide. The hydrolysis of the cyclic-mide yields Asp- and isoAsp-drugs, and the racemization of cyclic-imide hydrolysis and racemization reactions kinetically and by <sup>18</sup>O exchange experiments using <sup>13</sup>C-NMR, to elucidate the mechanisms of both formation and breakdown of this intermediate. Thesis Advisor: Richard L. Schowen, Ph.D., Summerfield Distinguished Professor, Pharmaceutical Chemistry.

#### **POSTDOCTORAL RESEARCH FELLOWSHIPS IN PHARMACEUTICS**

Complementing the other two pharmaceutics programs offered by the PhRMA Foundation is the Postdoctoral Research Fellowships in Pharmaceutics entering its fourth 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 recognizes the critical need for such well-trained scientific investigators. Each postdoctoral award gives \$25,000 per year for two years. Eight awards have been made since inception.

#### In 1995, the following individual received an award:

**Kathleen M. Hillgren, Ph.D.,** School of Pharmacy, University of California, San Francisco, School of Pharmacy: "Oral Absorption of Peptidic Drugs." A major obstacle to the widespread use of peptidic drugs is the poor oral availability of these molecules. The overall objective is to define the parameters that control the transport of bile acid-peptide conjugates at the 24 position through the intestinal and hepatic bile acid transporters. Small peptides coupled to the 24 position of cholic acid show affinity for and are transported by the bile acid carrier in Caco-2 cell monolayers, a model for absorptive



intestinal enterocytes. This laboratory will establish a cell culture transport system to study bile acid transport through hepatocytes on monolayers and use it to compare transport of bile acid-peptide conjugates through these cell types. This strategy may allow peptidic drug absorption; however, if the peptides are to be active, the bile acid moiety should not be detrimental to the drug effect. If it does interfere with drug action, the bile acid must be separated from the peptide after absorption. Thus a second goal is to develop a prodrug strategy that permits the peptide to be enzymatically separated from the bile acid. Understanding of the transport parameters in the two major cell types that transport bile acids might assist the development of bile acid system for the oral delivery of peptidic drugs.

#### Entering the second year of their award in 1995 are:

**Srinivasan Venkatesh, Ph.D.,** School of Pharmacy, University of Utah: "Influence of Compositional and Morphological Heterogeneity on Equilibrium Distribution and Kinetics of Drug Transport in Parenteral Emulsions."

#### Ending their awards in 1995 are:

**Jeffrey A. Hughes, Ph.D.,** School of Medicine, University of North Carolina at Chapel Hill. Dr. Hughes accepted an appointment as Assistant Professor with the University of Florida.

**Kenneth R. Phares, Ph.D.,** School of Pharmacy, University of North Carolina, Chapel Hill: "*In Vitro* Cell Monolayer Model for Investigating Folate Receptor-mediated Transcytosis." Dr. Phares ended his award early to accept a position with AAI Inc. of Wilmington, N.C.

Lawrence Ka-Yun Ng, Ph.D., University of Kansas, School of Pharmacy. Dr. Ng received an appointment as Assistant Professor at University of Colorado HSC.

### Pharmacoeconomics

#### FACULTY DEVELOPMENT AWARDS IN PHARMACOECONOMICS

There is widespread concern about rising healthcare expenditures as well as increasing interest in understanding the impact of new therapies on patient-focused outcomes such as mortality, functional status and quality of life. Because of these new perspectives, choices about new drugs are now based not only on traditional safety and efficacy measures but also on patient-assessed efficacy and economic values measures. A drug development program needs to include all of the outcome measures so that the information needs of the different decision makers can be met. Taking this into consideration, the PhRMA Foundation, recognizing the need for manpower to perform these outcome analyses, has implemented its Faculty Development Awards in Pharmacoeconomics program. Three awards were given for 1995 and each award offers \$40,000 annually for two years.

#### The following individuals received awards beginning July 1995:



**Karen Ann Sauer, Pharm.D.,** Assistant Professor, College of Pharmacy, University of Arizona: "(1) A Cost-Benefit Analysis of Four Hormonal Contraceptive Methods." The purpose of this project will be to evaluate the relative cost-effectiveness of four hormonal contraceptive agents. A second study is designed to assess the value of a compliance-enhancing intervention for patients with hypertension or diabetes mellitus.

(2) "The Financial Impact of OBRA '90 on Community Pharmacies." The study will assess direct pharmacy costs expended to meet the OBRA '90 mandate.



**Kevin A. Schulman, M.D.,** Assistant Professor, School of Medicine, Georgetown University: "Methods of Prospective Economic Assessment." Dr. Schulman's project will focus on the development of methods to assess health-related quality of life in clinical trials and the development of economic methods to help determine the appropriate time period for clinical evaluation of a new pharmaceutical therapy. Analysis will center upon the development of specific functions, tests or conditions that should be required in order to report statements about the efficacy of a therapy from a pharmacoeconomics perspective.



Jane C. Weeks, M.D., Assistant Professor, Dana Farber Cancer Institute, Harvard Medical School: "Validation of a New Method for Measuring Utilities for Pharmacoeconomic Studies in Cancer." Because quality of life is difficult to measure, it is often not evaluated in pharmacoeconomic studies. This project will develop and test a new and practical way to measure quality of life for use in pharmacoeconomic studies of cancer treatments. The validity of the resulting formula will be assessed by comparing the utilities it generates with utilities elicited directly from respondents in the

validation study and from patients in several ongoing cancer clinical trials.

### **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.

### **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**

Research Starter Grants are intended to provide financial support for beginning investigators. The program, in 1995, allowed for 11 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 488 research starter grants have been made, including the 11 awards beginning January 1, 1995.

#### Sandra Bajjalieh, Ph.D.,

University of Washington School of Medicine "Molecular Mechanisms of Neurotransmission"

#### Michael Philip Gosland, Pharm.D.

University of Kentucky College of Medicine "Evaluation of the Role for Multidrug Resistance (MDR) Genes in Normal Human Lymphocyte Function"

#### Kalpana R. Kamath, Ph.D.

South Dakota State University College of Pharmacy "Islets of Langerhans in Gellan Microcapsules as Bioartificial Pancreas"

#### Lin Mei, M.D., Ph.D.

University of Virginia School of Medicine "Mechanisms of the Regulation of Protein Tyrosine Phosphatases at the Neuromuscular Junction"

#### Elizabeth A. Pehek, Ph.D.

Case Western Reserve University School of Medicine "Effects of Serotonin Receptor Agonist and Antagonist Drugs on Cortical Dopamine Release"

#### Rhoda A. Reddix, Ph.D.

Louisiana State University, New Orleans School of Medicine "Pharmacological Management of Secretory Diarrhea: Role of Nitric Oxide, Endothelin-1 and Prostaglandins in Cholera Toxin-Induced Intestinal Secretion"

#### Yao Sun, M.D., Ph.D.

University of Missouri Columbia School of Medicine "A Local Angiotensin System and Tissue Repair in the Rat Heart" Bonita Gay Taffe, Ph.D. Wayne State University School of Medicine "The Role of Nitric Oxide in DNA Damage and Repair"

Mark M. Voigt, Ph.D. School of Medicine Saint Louis University "Investigation of the Molecular and Cellular Biology of 5-Hydroxytryptamine<sub>1</sub> Receptor" Hermann von Grafenstein, M.D., Ph.D. University of Southern California School of Pharmacy "Mannosylated Peptides as Candidate Vaccines and Probes for Mannose Receptor Function"

Dianqing Wu, Ph.D. University of Rochester School of Medicine and Dentistry "Specific Interactions Between G. Proteins and PLC"

Based on need for funds, a review of the 17 research starter grantees whose awards began January 1, 1994, for a second year of the awards resulted in six of them having their awards continued. These are:

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

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

Henry C. Farrar, M.D. University of Arkansas College of Medicine **Dale G. Hoyt, Ph.D.** University of Pittsburgh School of Medicine

**Calvin M. Johnson** University of Florida College of Medicine

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



President Maurice Q. Bectel addresses the Annual Awardee Meeting General Session on February 9, 1995.

# Purpose

Celebrating 30 Years



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 27 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.

Celebrating 30 Years

# Report of the Treasurer



**Mr. G. Gilbert Cloyd** Secretary-Treasurer PhRMA 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 1994 was \$2,248,368. Of this amount, \$1,836,600 came from contributions; \$100,000 was brought in from the over-funded Future Commitment Fund to kick off the

new Pharmacoeconomics Program; and the balance of \$311,768 came from investments and refunds of unexpended balances from grants.

In 1994, grant expenses totaled \$1,944,525; Foundation Annual Awardee Meeting and ASPET meeting expenses amounted to \$72,924; Honoraria totaled \$45,900 and Professional Services totaled \$38,866; Committee Meeting expenses amounted to \$80,115; special projects and other expenses for 1994 amounted to \$384,623. The total fund balance as of December 31, 1994 was \$4,702,862. 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, 1994, the contingency liability for 1995-98 was \$3,374,851.

The Foundation's financial position as of December 31, 1994, has been audited by the Washington DC accounting firm of Buchanan & Company.

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**G. Gilbert Cloyd** Secretary-Treasurer PhRMA Foundation and Vice President, Pharmaceuticals Procter & Gamble USA The Procter & Gamble Company

#### STATEMENT OF INCOME AND EXPENDITURES FOR THE YEAR ENDED DECEMBER 31, 1994

#### Income

Contributions Interest from Investments Interest Transferred from Future	\$1,836,600 95,076 185,335
Commitment Fund Funding for New Pharmacoeconomics Program from Future Commitment Fund Miscellaneous Income	100,000 <u>31,357</u>
Total Income	\$2,248,368
Expenditures	
Grants—Note A Clinical Pharmacology Unit Award Faculty Awards in Clinical Pharmacology Faculty Awards in Basic Pharmacology Fellowships for Careers in Clinical Pharmacology Advanced Predoctoral Fellowships in Pharm/Tox Pharmacology-Morphology Fellowships Medical Student Research Fellowships Research Starter Grants Faculty Awards in Toxicologic-Pathology Advanced Predoctoral Fellowships in Pharmaceutics Undergraduate Fellowships in Pharmaceutics Postdoctoral Fellowships in Pharmaceutics	\$91,068 380,000 180,000 104,886 305,500 133,098 62,500 362,500 125,500 125,500 129,473
Grant Total	\$1,944,525
Administrative	
Annual Awardee Meeting and ASPET Meeting Committee Meetings and Travel Special Projects Honoraria Publications Office Expense Professional Services Rent, Salaries, Taxes	
Administrative Total	622,428
TOTAL EXPENDITURES	\$2,566,953
Excess of expenditures over income Operating fund balance at January 1, 1994 Operating fund balance December 31, 1994 Future Commitment Fund (Reserve Fund) (Note B)	\$(318,585) 2,849,324 2,530,739 2,172,123
Total Fund Balance at December 31, 1994	\$4,702,862
Note A–In addition to the amounts shown, the Foundation is committed, subject to annual review, to make certain grants. At December 31, 1994, the amounts still to be disbursed with respect to these grants amounted to aggregated \$3,374,851 with \$1,061,034 of this to be disbursed during 1995; \$2,134,317 in 1996; \$179,500 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 Interest Transferred to Operating Fund Dividend Income Gain (Loss) on Sale of Stock Less: Trust Commission Expense Less: Funding for New PCO Program	
Excess of Expenditures Over Income:	(141,244)
Future Commitment Fund Balance at January 1, 1994 Future Commitment Fund Balance at December 31, 1994	2,313,367 <b>\$2,172,123</b>

Celebrating 30 Years

# Organization and Administration

The PhRMA Foundation operates through its Officers, Board of Directors and six advisory committees. In March of 1995, Mr. Robert C. Black, President of Zeneca Pharmaceuticals Group, was elected Chairman. Mr. G. Gilbert Cloyd, Vice President, Pharmaceuticals, Procter & Gamble USA, was elected Secretary-Treasurer. The Office of Vice-Chairman was temporarily left vacant due to the restructuring of several PhRMA member companies. Mr. Philip R. Tracy, President and Chief Executive Officer of Burroughs Wellcome Co., retired as Chairman of the Foundation Board—having filled the unexpired term of Charles Saunders, M.D., then-Chairman of Glaxo Inc. Dr. Sanders retired from the PhRMA Foundation Board as of December 1994.

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. Arthur H. Hayes (L), former awardee and former Commissioner of the Food and Drug Administration, Donna Moore, Foundation Director of Programs, and Morry Bectel, Foundation President, discuss the current activities of the Foundation.Dr. Hayes currently serves as President of MediScience Associates and member of the Foundation's Scientific Advisory Committee.

#### **1995 OFFICERS**



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\*joined the Foundation Board in December 1994 \*\*joined the Foundation Board in February 1995



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Professor Emeritus Department of Pharmacology University of Minnesota Medical School Minneapolis, Minnesota

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Director Department of Immunology Marion Merrell Dow Research Institute Cincinnati, Ohio

\*Frank Standaert, M.D., member of the BPAC since 1973, and member of the SAC since 1992, died on March 17, 1995.

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

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#### John E. Eisenberg, M.D. Chairman Department of Medicine Georgetown University School of Medicine Washington, DC

#### Jean Paul Gagnon, Ph.D.

Director of Industry Affairs Marion Merrell Dow Inc. Kansas City, Missouri

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Director of Epidemiology and Outcome Research Parke-Davis Pharmaceutical Research Ann Arbor, Michigan

#### Raymond Townsend, Pharm.D.

Vice President International Applied Health Care Research Glaxo Wellcome Inc. Research Triangle Park, North Carolina



Terrence Blaschke, M.D. (R), Stanford University School of Medicine, and Dan Gretler, M.D., have front-row seats at the February 9 PhRMA Foundation Annual Awardee Meeting General Session. Dr. Blaschke, a former awardee, now serves on the Clinical Pharmacology Advisory Committee. Dr. Gretler is a former awardee, having received two Foundation awards—the Postdoctoral Fellowship and Faculty Development Award in Clinical Pharmacology.

# Benefactors

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### PhRMA Member Companies and Company Foundations

#### **OVER \$3 MILLION**

\*Hoffmann-La Roche Inc. \*Bristol-Myers Squibb Foundation Bristol-Myers Squibb Company

#### **OVER \$2 MILLION**

The Merck Company Foundation Merck & Co., Inc. Merck Human Health Division \*Warner-Lambert Foundation Warner-Lambert Company Parke-Davis \*American Home Products Corporation

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#### **OVER \$500,000**

\*Sanofi Winthrop \*Bayer Corporation \*Marion Merrell Dow, Inc. \*Zeneca Pharmaceutical Group

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Relaxing during the Annual Awardee Banquet are three members of the Basic Pharmacology Advisory Committee, Bernard Mirkin, M.D., Ph.D., Northwestern University and Children's Memorial Institute, Dr. Frank Standaert, NIH Special Expert, Frederick M. Radzialowski, Ph.D., FMR Research Associates. (Dr. Standaert died unexpectedly on March 17, 1995. A portion of this Annual Report is dedicated to his memory.)

# Applications

Celebrating 30 Years



Descriptive brochures and application forms for all of the PhRMA Foundation Grant Programs listed on page 44 are available by contacting the Foundation offices.

For more information, please write to:

#### 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 1996

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)	4 budgeted/ 3 months to 24 months	\$ 40,000 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	<ul> <li>\$ 120,000 total</li> <li>\$ 30,000 per award per year</li> </ul>	September 15 December 15 July 1
(5) Research Starter Grants (1972)	11 budgeted/ 2 years	<ul> <li>\$ 275,000 total</li> <li>\$ 12,500 per award per year</li> </ul>	September 1 December 15 January 1
(6) Advanced Predoctoral Fellowships in Pharmacology/Toxicology (1978)	9 budgeted/ 1 or 2 years	<ul> <li>\$ 225,000 total</li> <li>\$ 12,500 per award per year</li> </ul>	September 15 December 15 January-August
Pharmacology-Morphology Advisory Committee			
(7) Fellowships in Pharmacology-Morphology including Cell Biology (1968)	3 budgeted/ 2 years	<ul> <li>\$ 129,000 total</li> <li>\$ 21,500 per award per year</li> </ul>	January 15 March 15 July 1
Pharmaceutics Advisory Committee			
(8) Advanced Predoctoral Fellowships in Pharmaceutics (1987)	5 budgeted/ 1 or 2 years	<ul> <li>\$ 125,000 total</li> <li>\$ 12,500 per award per year</li> </ul>	October 1 December 15 January-August
(9) Undergraduate Research Fellowships in Pharmaceutics (1990)	7 budgeted/ 1 year	\$ 35,000 total \$ 5,000 per award	October 1 December 15 January-July
(10) Postdoctoral Fellowships in Pharmaceutics (1992)	1 budgeted/ 1 or 2 years	<ul> <li>\$ 50,000 total</li> <li>\$ 25,000 per award per year</li> </ul>	October 1 December 15 January-December
Pharmacoeconomics Advisory Committee			
(11) Faculty Awards in Pharmacoeconomics (1995)	2 budgeted/ 2 years	<ul> <li>\$ 160,000 total</li> <li>\$ 40,000 per award per year</li> </ul>	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

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