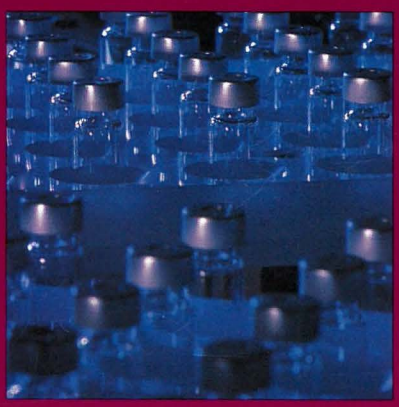
1993 Annual Report

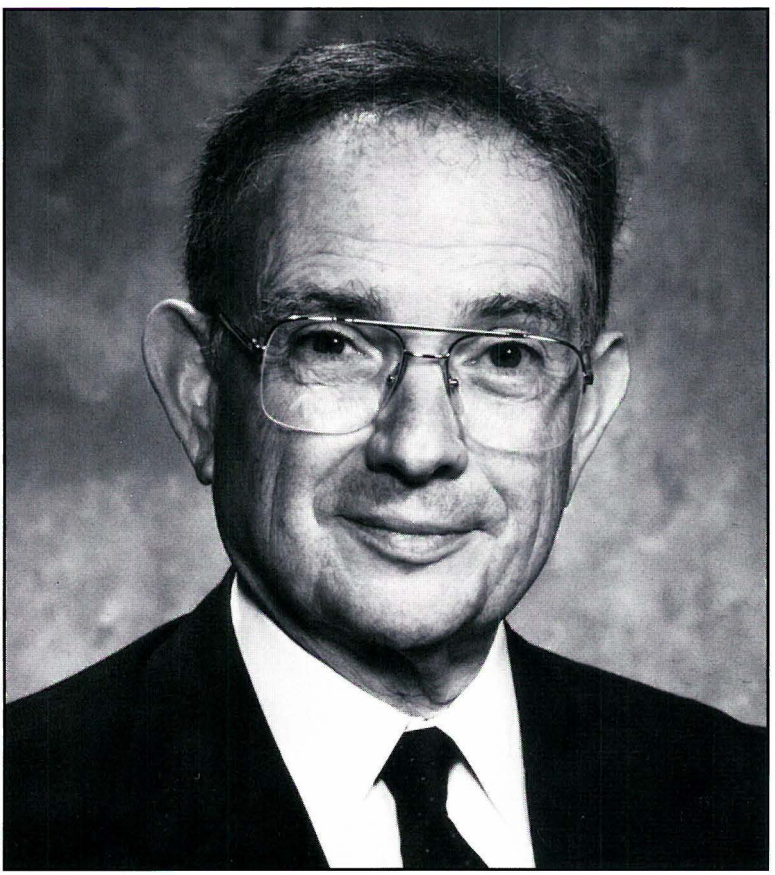


Pharmaceutical Manufacturers Association Foundation

1993 Annual Report

Pharmaceutical Manufacturers Association Foundation

Dedicated to



Theodore Cooper

(1928-1993)

Theodore Cooper, M.D., Ph.D. was a man of many achievements, one whose leadership and dedication to advancing the health of the nation and its people are legendary. Born December 28, 1928, Ted Cooper passed away April 22, 1993, of bone marrow cancer.

Dr. Cooper's career had placed him at the crucial places at the precise critical time for him to make the maximum–and ideal–contribution to the issue at hand. A considerable number of efforts–this Cooper Committee, that Cooper Report–provide historical documentation of his contributions, including those he made specific to the affairs of the Pharmaceutical Manufacturers Association Foundation, including serving as Vice Chairman of the Foundation Board at the time of his death.

A heart surgeon who published more than 200 scientific articles, Dr. Cooper served as Director of the National Heart and Lung Institute of NIH, followed by a term as Assistant Secretary of Health, Education and Welfare in the Ford Administration. Either in his government positions or in scientific advisory committee posts, he had considerable influence in developing pubic health policies affecting such areas as nutrition, AIDS, swine flu vaccine, and heart disease. A special tribute was published in a medical device industry publication acknowledging his key role in developing the legislative principles by which FDA was given authority to regulate the marketing of medical devices; his reward was being present for the presidential signing of that legislation in 1976.

His involvement with the drug industry extended over a number of years, having served on The Upjohn Company board of directors beginning in 1974. In 1980, he turned down an offer for a high-level appointment as he had just started with The Upjohn Company. In 1987, he became Chairman of Upjohn's Board and Chief Executive Officer, the post he held until 1993.

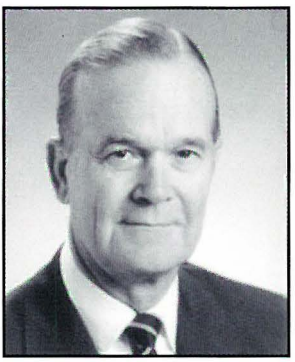
For his many contributions to public health, to the industry, and to the Foundation, this 1993 Annual Report is dedicated to Theodore Cooper, M.D., Ph.D.

For those wishing to make a memorial contribution, the family has designated Kalamazoo's New Museum. Contributions may be made to:

The New Museum
c/o KVCC Foundation
6767 West O Avenue
Kalamazoo, MI 49009

Contents

Report of the Chairman



Charles A. Sanders, M.D.
Chairman, PMA Foundation

Last year, during the Foundation's "silver anniversary," I reported the pride I felt to be Board Chairman at that time and how smoothly the transition from one Chairman to another had been. Entering my second year as Chairman, I am now even more enthusiastic about the mission and activities of the Foundation.

The Foundation's activities and accomplishments continue. The reports of activities, awardees, and officers contained in the 1993 Annual Report of the Pharmaceutical Manufacturers Association Foundation will give you a sense of why I maintain my enthusiasm.

1993 has also been a year of loss. The passing of Ted Cooper is especially painful and this *Annual Report* is dedicated to his memory. He served the Foundation superbly, not only as a generous contributor through The Upjohn Company but as Vice Chairman of the Foundation Board of Directors at the time of his death. The Foundation will miss his leadership and wisdom; I miss his friendship.

The 1992-1993 year has been another successful one for the Foundation. The reports of President Maurice Q. Bectel and Secretary-Treasurer Robert C. Black are included in this *Annual Report* as a permanent record of the administrative and financial affairs of the Foundation. Mr. Black, President of ZENECA Pharmaceuticals Group, was elected to the post of Secretary-Treasurer at the March, 1993, Board Meeting, succeeding Joseph A. Mollica, Ph.D., who had served in that capacity since 1989.

Also serving the Foundation as members of the Board of Directors for 1993-1994 are:

- **Mr. Phillip R. Tracy**, President and Chief Executive Officer, Burroughs Wellcome Co., who was named to fill Dr. Cooper's unexpired term as Vice Chairman.
- **Paul N. Clark**, Senior Vice President, Pharmaceutical Operations, Abbott Laboratories
- **G. Gilbert Cloyd**, Vice President, Pharmaceuticals, Procter & Gamble USA
- **Jan Leschly**, Chairman, SmithKline Beecham Pharmaceuticals
- **Herbert Sosman**, President, Wallace Laboratories
- **Sidney A. Taurel**, Executive Vice President and President, Pharmaceutical Division, Eli Lilly and Company
- **Robert N. Wilson**, Vice Chairman, Board of Directors, Johnson & Johnson
- **Gerald J. Mossinghoff**, President, Pharmaceutical Manufacturers Association, serves *ex-officio*.

Concluding their terms on the Foundation Board in March, 1993 were:

- **Sheldon G. Gilgore**, M.D., Chairman and Chief Executive Officer, Searle, who concluded a term as Immediate Past Chairman of the Foundation Board.
- **Joseph A. Mollica**, Ph.D., President and Chief Executive Officer, DuPont Merck Pharmaceutical Company, who concluded his fourth term as the Foundation's Secretary-Treasurer.
- **George J. Sella, Jr.**, Chairman and Chief Executive Officer, American Cyanamid.

My appreciation is also extended to those who have served the Foundation so ably in the past, especially those whose terms have just expired. My welcome is extended to the new members of the Board who join those of us who have served before.

The principal objective of the Foundation is quite straightforward: to support and encourage capable young scientists in the pursuit of a career in biomedical research. Without them—whether in government, academe, or industry—the advancement of healthcare through the discovery and development of new pharmaceuticals would be more than compromised, there would be none.

And so, in this twenty-sixth year of the PMA Foundation's history, we salute the 70 awardees of Foundation grants for 1993. The names, titles and research descriptions of these awardees' and the amounts of their stipends are listed on the following pages. They and their projects follow the traditions of

the Foundation award recipients over the previous twenty-five years. Join with me and the Foundation Board in extending them our congratulations and best wishes.

Join with us too in expressing our appreciation to the members of the Foundation's Advisory Committees. These scientists from academe and industry—some of them previous awardees themselves—contribute of their time and expertise in making the Foundation's Awards Program a respected mechanism for recognizing and supporting deserving young scientists and worthwhile research projects.

As Chairman of the Foundation Board of Directors, let me express appreciation to the more than 100 research-intensive companies which are members of the Pharmaceutical Manufacturers Association, and the associate members and research affiliates, as well. It is the contributions of these firms, showing their dedication to the advancement of healthcare, which make the work of the PMA Foundation possible.

Charles A. Sanders, M.D.
Chairman, PMA Foundation
Chairman and Chief Executive Officer
Glaxo Inc.

Report of the President

Maurice Q. Bectel, D. Sc.
President

The 1993 *Annual Report* of the Pharmaceutical Manufacturers Association Foundation provides us with an opportunity to assess events and trends, analyze the data of the past year, and present the Foundation's 1993 awardees and their research.

It is not by coincidence that this PMA Foundation *Annual Report* is dedicated to the memory of Ted Cooper. Not only was Dr. Cooper serving as Vice Chairman of the Foundation Board, but he had been a major contributor to the Foundation, its activities, its structure, and indeed, its very existence. During the mid-1980s, an intensive review of the Foundation was undertaken, with Ted Cooper as Chairman of the review committee. The resultant "Cooper report" reset the course for the Foundation. He and his counsel shall be missed by all of us but certainly one of his major beneficiaries is the PMA Foundation.

In total consistency with the primary objective of the Foundation—encouraging the education and training of young researchers in the biomedical sciences—the Foundation's major activity is the awarding of grants and scholarships to these who qualify. The record of those achievements is maintained, not just in the Foundation's files, but through the following pages of this *Annual Report*. These are the people whose research projects have passed the scrutiny of a rigorous scientific review process and who have been named recipients of the Foundation's grants. Copies of this report are distributed to many interested parties beyond the Foundation's immediate constituencies, including the press and Congress.

We are proud to list in the 1993 *Annual Report* over 70 award recipients and summaries of their research projects. These awardees will receive more than $2 million in grants and

scholarships within the eleven categories of scientific endeavor supported by the Foundation's grant program. Collectively, they represent the greatest pride of the Foundation–and the greatest source of hope for future achievements in the field of therapeutics. Copies of program brochures for each of the eleven PMA Foundation grants are available on request from the Foundation office.

Despite the impressive number of recipients and the aggregate sum of the awards, neither is a record. Reflective of the world economy and internal competition, sales in the pharmaceutical industry have remained relatively flat. Worse yet, because it is specific to the pharmaceutical industry, in excess of a billion dollars in shareholder equity has been lost during early 1993 through reductions in stock valuation. Resultant downsizing of personnel within the industry means fewer opportunities for new scientists and researchers. Difficult times for the industry also means these firms have diminished ability to support the Foundation and its programs, although I am pleased to report that, by and large, the research-intensive member companies of the Pharmaceutical Manufacturers Association have placed the Foundation on a high priority and their support generally continues unabated.

But growth in the industry and the Foundation is necessary for true progress. Despite the fact that some 255 applicants were submitted–virtually all qualified and worthy of funding–only 70 awards were actually funded for 1993. Unfortunately, funding all applicants would exceed, by many times, the financial capacity of the Foundation. Without the continued growth of the research-intensive pharmaceutical industry, it loses its capability to support a continued growth pattern for the Foundation. That means "flat" records in Foundation support for biomedical sciences and fewer positions and resources to attract this country's most capable young scientists.

And the bottom line in a lessened U.S. commitment to biomedical advancement is a delay in achieving success in such health problem areas as cancer, AIDS, stroke, and other diseases and conditions.

Although greater resources could be put to good use, the Foundation continues to make progress and continues to gain recognition in foundation management circles as an organization to emulate. Activities are reported periodically in the newsletter, *Tracking 26, Scholars,* and this *Annual Report.*

In addition to publications, scientific review panels, and its Board and business meetings, the Foundation conducts an annual Awardee Meeting and a scientific program in conjunction with the American Society for Pharmacology and

Experimental Therapeutics (ASPET) annual meeting.

- The Foundation's ASPET meeting and reception were held August 17, 1992, in Orlando, Florida, with nearly 100 in attendance. The Keynote speaker for this event was Dr. Lawrence J. DeLucas, a member of the Columbia Space Shuttle Mission.
- The Awardee Meeting was held this year, as in the past, in Washington, DC. During February 17-18, 1993, over 100 award recipients, Advisory Committee members, and Foundation officials heard reports on research projects and viewed poster sessions describing their results.

These Foundation activities strengthen the relationships between the Foundation and its several constituencies, as well as provide greater visibility to the Foundation and its programs.

The internal affairs of the Foundation continue to function smoothly. Charles A. Sanders, M.D., Chief Executive Officer of Glaxo Inc., was elected to his second term as Chairman of the Foundation's Board of Directors. Philip R. Tracy, President and Chief Executive Officer of Burroughs Wellcome Co., has been named to complete the unexpired term of the late Dr. Cooper as Vice Chairman. Robert C. Black, President of ZENECA Pharmaceuticals Group, was elected to the post of Secretary-Treasurer. His report appears elsewhere in this *Annual Report.*

Please review the pages of this *Annual Report.* It represents a window into the future of biomedical science.

Maurice Q. Bectel, D. Sc.
President

On Record

Meetings and Other Activities

Twenty-Second Annual Awardee Meeting

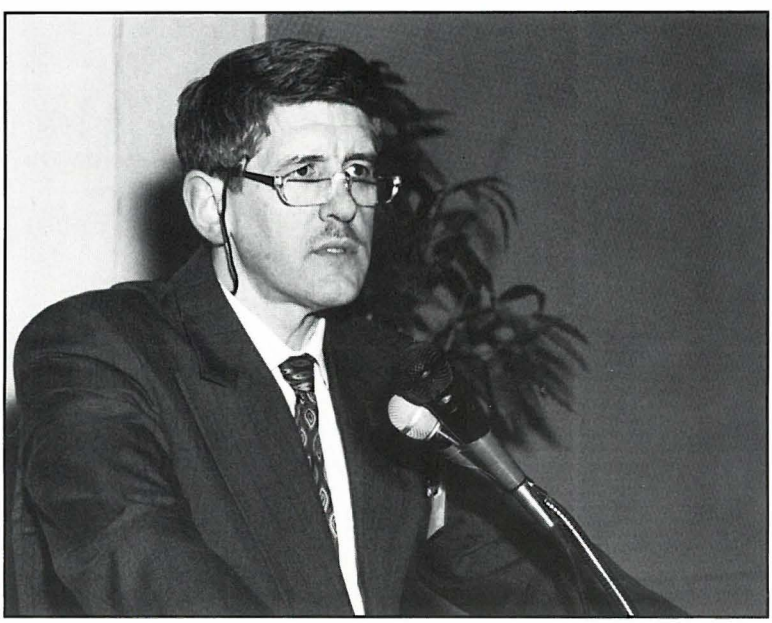
The PMA Foundation Annual Awardee Meeting was held on February 17 and 18, 1993, at the Washington Vista International Hotel, in Washington, D.C. Over 100 current and former awardees, as well as committee members from academe and

Foundation President Maurice Q. Bectel addresses the more than 100 attendees at the 1993 Annual Awardee Meeting, held in Washington, D.C. in February.

industry, and PMA Foundation staff were pleased to hear John S. Lazo, Ph.D., deliver the Thomas E. Hanrahan Memorial Lecture on "Anticancer Drug Resistance." The audience thoroughly enjoyed Dr. Lazo's informative and current presentation. Dr. Lazo is Allegheny Foundation Professor and Chairman of the Department of Pharmacology at the University of Pittsburh School of Medicine.

Preceding Dr. Lazo'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 pharmacolgy and pharmacology-morphology allowed attendees to hear presentations regarding their specific disciplines.

The Annual Awardee banquet was held on the evening of February 17 providing everyone with an opportunity to interact and relax before the official program February 18. The evening's events included an after-dinner presentation by Carl C. Peck, M.D., long-time friend of the PMA Foundation and Director of the Center for Drug Evaluation and Research of the Food and Drug Administration.



Carl. C. Peck, M.D., Director of FDA's Center for Drug Evaluation and Research, spoke warmly of the Foundation, its programs, and its awardees and participants after the Awardee Banquet on February 17.

PMA Foundation Board of Directors –New Members

At its March 29 meeting in Scottsdale, Arizona, the PMA Foundation Board of Directors elected officers, installed new Board members and said goodbye to retiring Board members. Charles A. Sanders, M.D., Chairman and Chief Executive Officer of Glaxo Inc., was re-elected Chairman. The late Theodore Cooper, M.D., Ph.D., Chairman and Chief Executive Officer of The Upjohn Company, had been elected Vice-Chairman. In light of Dr. Cooper's death in April, Mr. Phillip R. Tracy, President and Chief Executive Officer of Burroughs Wellcome Co., kindly agreed to fill the term as Vice Chairman. Mr. Robert C. Black, President of ZENECA Pharmaceuticals, was elected Secretary-Treasurer. Newly elected to the PMA Foundation Board of Directors are: Herbert Sosman, President, Wallace Laboratories, Sidney A.Taurel, Executive Vice President and President, Pharmaceuticals Division, Eli Lilly and Company, and Mr. Robert N. Wilson, Vice Chairman, Board of Directors, Johnson & Johnson.

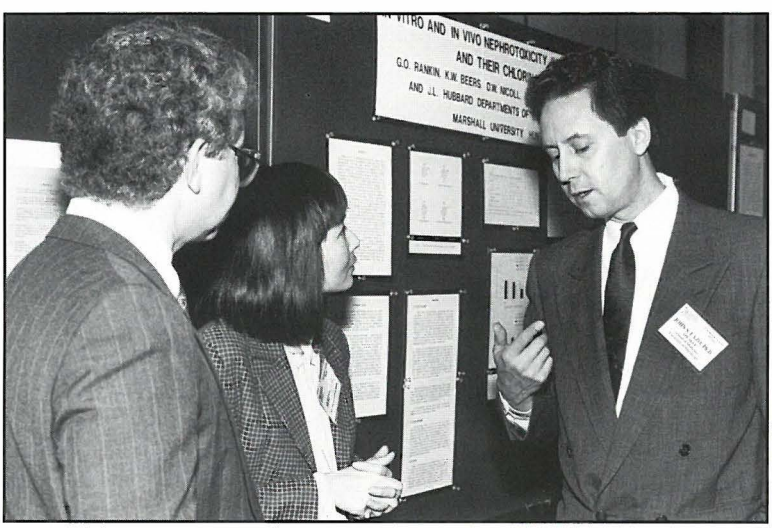
Retiring from the Board are: Sheldon G. Gilgore, M.D., Chairman and Chief Executive Officer, Searle. Dr. Gilgore served as Chairman 1990-92, and as Immediate Past Chairman 1992-93. Joseph A. Mollica, Ph.D., President and Chief Executive Officer, DuPont Merck Pharmaceutical Company, concluded his fourth term as Secretary-Treasurer; and George J. Sella, Jr., Chairman and Chief Executive Officer, American Cyanamid served three years on the Board.

Ten pharmaceutical company executives serve on the current Foundation Board of Directors along with Gerald J. Mossinghoff, President of the PMA, who is an *ex-officio* member. In addition to Sanders, Tracy, Black and new Board members Sosman, Taurel and Wilson, Board members serving are: Paul N. Clark, Senior Vice President, Pharmaceutical Operations, Abbott Laboratories; Mr. G. Gilbert Cloyd, Vice President, Pharmaceuticals, Procter & Gamble USA, and Mr. Jan Leschly, Chairman, SmithKline Beecham Pharmaceuticals.

Seventeenth PMA Foundation Program at ASPET

This year marked the last Fall meeting of the American Society for Pharmacology and Experimental Therapeutics, and thereby the last Fall PMA Foundation program which has taken place every year in conjunction with the ASPET meeting. Appropriately, the PMAF program attracted more than 90 attendees—current and former awardees, Pharmacology Department Chairmen, Advisory Committee members and ASPET officials. In fact, this scientific program was the most well attended PMAF/ASPET program of recent years.

Speaking at the 1993 program on Saturday, July 31, was Irwin D. Kuntz, Ph.D., Acting Chairman of the Department of Pharmaceutical Chemistry and Professor of Chemistry and Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco. Dr. Kuntz enlightened the audience with his remarkable presentation—replete with current overheads and slides—regarding "Computer Assisted Drug Design." E. (Eddie) Leong Way, Ph.D., longtime friend of Dr. Kuntz and the PMA Foundation, made the introductions.



During the Poster Session, Speaker John S. Lazo, Ph.D., was asked to amplify a point by awardees.

Education And Training Programs

The PMA Foundation's goals in education and research are accomplished through its eleven funding programs–four in clinical pharmacology, two in pharmacology/toxicology, one in the combined field of pharmacology-morphology, and three in pharmaceutics. 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

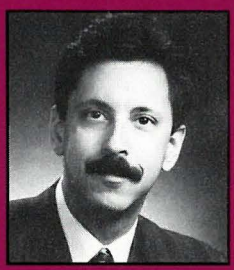
Faculty Awards in Clinical Pharmacology

The clinical pharmacology program provide four awards to students, fellows and faculty. 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, 1993, 98 individuals have been supported under this program since 1967.

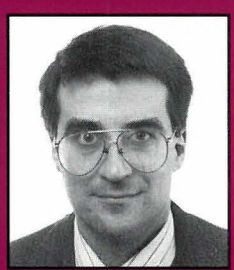
Recipients of the awards which began July 1993 are:

Evan D. Kharasch, M.D., Ph.D., Assistant Professor, Department of Anesthesiology, University of Washington, School of Medicine: "Human Anesthetic Toxicity: Mechanisms and Prevention." The research objective of this study is to enhance the safety of inhaled anesthetic agents by diminishing their toxic side effects. The mechanisms of anesthetic toxicity will be identified and clinical strategies devised for using protective treatments to diminish these side effects. This research will be accomplished by elucidating mechanisms of anesthetic bioactivation and clinical pharmacology of anesthetic toxification. Halothane, the most widely used anesthetic agent, is known to cause a rare but fatal fulminant hepatic necrosis. Fluorinated ether anesthetics such as methoxyflurane, enflurane and sevoflurane are defluorinated, releasing free fluoride ion which is nephrotoxic. The toxicity of all these anesthetics is intrinsically linked to their metabolism by hepatic cytochrome P450. The central hypothesis to be tested in this research is that specific isozymes of human cytochrome P450 are responsible for anesthetic toxification, and that selective inactivation of these isozymes can be accomplished clinically to diminish anesthetic metabolism and toxicity.



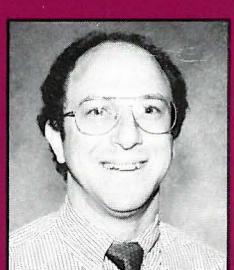
Evan D. Kharasch, M.D., Ph.D.

David W. Rudy, M.D., Assistant Professor, Department of Medicine, Indiana University, School of Medicine: "The Influence of Renal Function Upon the Stereospecific Pharmacokinetics and Pharmacodynamics of Non-steroidal Anti-inflammatory Drugs (NSAIDS)." This study involves two projects designed to further understand the pharmacokinetics and influence upon renal function of NSAIDs. A number of important pharmacologic considerations such as stereospecific metabolism and chiral inversion have recently been elucidated. This research will add to this knowledge by further evaluating the elimination of propionic acid NSAIDs in renal function. A complete understanding of the complex pharmacokinetics may lead to more rational dose recommendations of this important class of medications in patients with decreased renal function.



David W. Rudy, M.D.

Jason Gari Umans, M.D., Ph.D., Assistant Professor, University of Chicago Pritzer School of Medicine, "Endothelial Modulation of Small Artery Function in Human Disease." This study will elucidate mechanisms whereby endothelial cell modulation of small artery function is altered in two human disease states: endotoxemia and hypertensive pregnancy. The first project is designed to elucidate mechanisms whereby endotoxin impairs both endothelium dependent relaxation and smooth muscle contraction. Proposed studies, performed in cultured



Jason Gari Umans, M.D., Ph.D.

endothelial and vascular smooth muscle cells, isolated conduit and resistance size arteries, will determine cellular mechanisms mediating these vascular effects of endotoxin.

The second project focuses on morphological and contractile properties of omental resistance arteries obtained from the pregnant normotensive women and patients with preeclampsia undergoing cesarian deliveries, comparing results to those from nongravid subjects and gravidas with chronic hypertension.

Recipients of the award which began July 1992 are:

Joshua Olajide Atiba, M.B., Assistant Professor of Medicine and Pharmacology, University of California, Irvine.

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.

Those who entered the second year of their award in 1992 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.

Individuals who entered the third year of their award in 1992 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.

Enjoying a lighter moment at the Awardee Meeting reception are (1 to r) Donna Moore, the Foundation's Director of Programs, Joseph Foss, a 1980 faculty awardee at the University of Chicago, and Doug Roberts, a 1986 faculty awardee, now with the FDA Center for Biologics Evaluation and Research.

Individuals who ended their awards in 1992 are:

Daniel David Gretler, M.D., Instructor, University of Chicago School of Medicine (ended award early to take position with Syntex).

Patrick Taylor Horn, M.D., Ph.D., Assistant Professor, Committee on Clinical Pharmacology, University of Chicago.

Ralph A Kelly, M.D., Assistant Professor, Harvard Medical School.

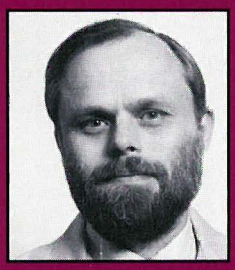
Lawrence G. Miller, M.D., Assistant Professor, Tufts University School of Medicine.

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 1993 may request that the fellowship begin July 1994 or July 1995.

The program began in 1973 awards under this program were made in 1973. Since that time, 56 fellowships have been awarded.



Merlin R. Hamre, M.D., M.P.H.

Recipient of the award beginning July 1, 1993:

Merlin R. Hamre, M.D., M.P.H., Northwestern University, Medical School: "The Relationship Between Nucleoside Analogue Transport Across Cell Membranes, Cytotoxicity and Development of Drug Resistance." This study will analyze the uptake of a specific class of cancer chemotherapeutic agents called nucleoside analogues into tumor cells to determine if inhibition of uptake influences the selectivity of their toxic action on tumor cells. Additionally, this study will determine the mechanism of resistance of neuroblastoma tumors to nucleoside analogues.

Recipient of the award beginning January 1992:

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

Individuals who entered the second year of their awards in 1992 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., Thomas Jefferson University, Jefferson Medical College. Dr. Terzic transferred his fellowship to Mayo in February 1992.

Sharing a moment at the reception are PMA Foundation President Bectel and Ted Brody, longtime member of the Basic Pharmacology Advisory Committee and Professor and Former Chairman of the Department of Pharmacology at Michigan State University.

Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology

The 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 fourteen awards have been made since 1974.

Individuals whose awards began in July 1993 are:

Michelle Brown, Louisiana State University, School of Medicine in New Orleans (one year)—"Effects of Burn Injury on Cardiovascular Function." Ms. Brown's principal advisor is Howard Lippton, M.D., Assistant Professor, Pharmacology and Internal Medicine.

Stephen Douglas Brown, University of Utah, School of Medicine (six months)—"Effect of the Novel Anticonvulsant Topiramate on $GABA_A$ Receptor Function." Mr. Brown's fellowship supervisor is H. Steve White, Ph.D., Assistant Professor, Pharmacology and Toxicology.

Kenneth J. Colley, Georgetown University, School of Medicine (one year)—"Antisense Inhibition of the Tumor Growth and Angiogenesis Factor Pleiotrophin (PTN)." Mr. Colley's principal advisor is Anton Wellstein, M.D., Ph.D., Associate Professor of Pharmacology and Medicine.

Simon Finger, Tulane University, School of Medicine (one year)—"Endothelial-derived Products Regulate the Pulmonary Circulation." Mr. Finger's principal advisor is Albert L. Hyman, M.D., Professor of Pharmacology, Medicine and Surgery.

Bradley S. Miller, Medical University of South Carolina, College of Medicine (one year)—"Identification of IGF-1 Regulated Nuclear Protein Kinases." Mr. Miller's fellowship advisor is Steven A. Rosenzweig, Ph.D., Associate Professor of Pharmacology.

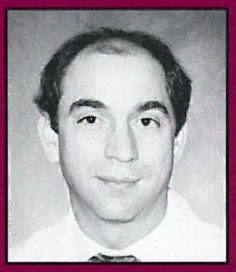
Hassan Movahedi, University of California, Irvine, College of Medicine (one year)—"Vasoconstrictor Synergism Between Serotonin and Norepinephrine." Mr. Movahedi's principal advisor is Ralph E. Purdy, Ph.D., Associate Professor of Pharmacology.

Charles Weaver, Boston University, School of Medicine (one year)—"Effect of Steroid Hormones on NMDA Mediated Cell Death in Rat Hippocampal Cells, *In Vitro* and *In Vivo*." Mr. Weaver's Fellowship Supervisor is David H. Farb, Ph.D., Chairman, Department of Pharmacology and Experimental Therapeutics.

Ethan Wiener, Columbia University, College of Physicians and Surgeons (one year)—"Molecular Interactions Mediating T-B Lymphocyte Collaboration." Mr. Wiener's principal advisor is Dr. Leonard Chess, Chairman, Department of Immunology.

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-four.



Mark J. Ratain, M.D.

Mark J. Ratain, M.D., Associate Professor of Medicine and Chairman, Committee on Clinical Pharmacology, University of Chicago, School of Medicine. The Committee on Clinical Pharmacology at the University of Chicago is a multidisciplinary group of investigators who participate in research geared towards developing and testing new therapeutic agents both within their various specialties and collaboratively across departmental boundaries. Ongoing research includes studies of an opioid receptor antagonist for anti-emetic effects, antineoplastic drugs, new therapies for asthma, treatments for gastrointestinal diseases, and determinants of drug use and abuse.

Basic Pharmacology

Faculty Development Awards in Basic Pharmacology

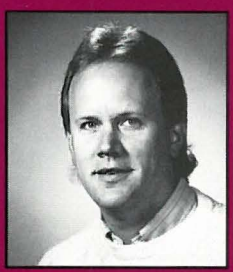
This Faculty Development Award was initiated to strengthen basic pharmacology by helping to maintain existing academic capability and, ultimately, to expand the field by enlarging the faculty base. To meet this goal, support is provided to full-time junior faculty members who give promise of outstanding 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 59.

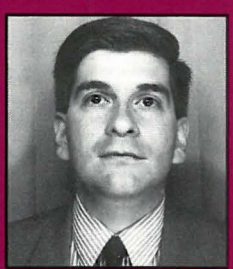
Recipients of the 1993 Faculty Development Awards in Pharmacology are:

Mark Leid, Ph.D., Assistant Professor, Oregon State University, College of Pharmacy: "Molecular Cloning and Functional Characterization of Mouse Retinoid X Receptor Isoforms." The goal of this research is to provide insight into the molecular mechanisms of retinoic acid (vitamin A) signal transduction. Cellular effects of retinoic acid are mediated by two classes of receptor proteins: retinoic acid receptors and retinoid X receptors. This project will examine the functional properties of retinoid X receptor isoforms and the potential role(s) of these proteins in the vitamin A signaling pathway.



Mark Leid, Ph.D.

Elias Lolis, Ph.D., Assistant Professor, Department of Pharmacology, Yale University, School of Medicine: "Molecular Mechanisms of Erythropoiesis and Erythroleukemia." The erythropoietin receptor mediates the normal production of red blood cells by erythropoietin, but is also involved in the induction of erythroleukemia. Erythropoiesis is initiated when the glycoprotein hormone binds to its receptor on the surface of hematopoietic cells. Virus-induced erythroleukemia is initiated by the physical association between the viral protein gp55 and the erythropoietin receptor. Despite the importance of these two processes, very little is known about the interactions between the proteins involved. The aim of this research is to identify and characterize the interactions using the tools of molecular biology, cellular immunology and X-ray crystallography.



Elias Lolis, Ph.D.

Bih-Hwa Shieh, Ph.D., Assistant Professor, Department of Pharmacology, Vanderbilt University, School of Medicine: "Role of InaD in Phototransduction: A Model for Examining the Phospholipase C/C-Kinase Cascade Regulated by Neurotransmitters." The objective of this research is to understand how InaD acts to regulate phototransduction in *Drosophila*. The InaD gene was isolated by subtractive hybridization. Preliminary characterization of InaD indicates that it is a membrane-associated protein expressed exclusively in photoreceptor cells. The regulation of InaD membrane association as examined by extracting the protein with and without detergent in wild-type and visual mutants will be investigated. Furthermore, to identify and characterize proteins that interact with InaD, a number of procedures including

Bih-Hwa Shieh, Ph.D.

affinity chromatography and the ligand overlay technique will be employed to understand the mediators and regulators of InaD in the visual cascade. Knowledge on the role of InaD in visual transduction will shed light on other G protein-coupled signal transduction mechanisms regulated by neurotransmitters.

Individuals who began their awards in July 1992 are:

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.

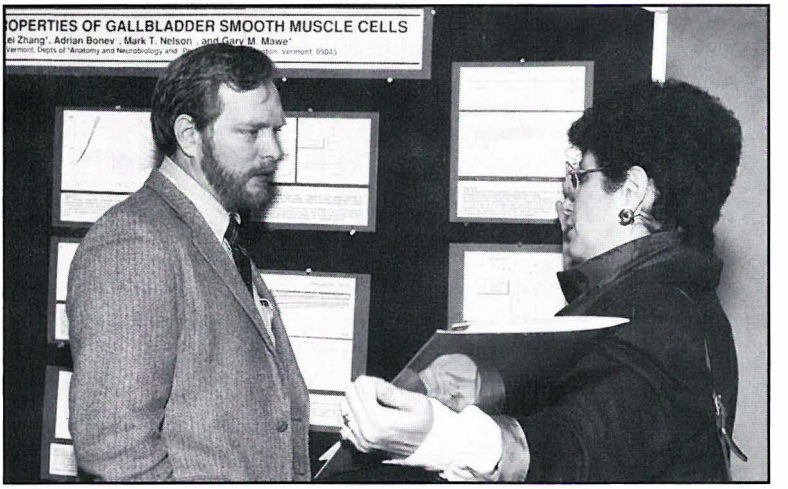
William Frederick Wonderlin, Assistant Professor, Department of Pharmacology and Toxicology, West Virginia University.

Entering their second year in 1992 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.



Gary Mawe, Ph.D. and Cheryl Dreyfus, Ph.D., both former pharmacology/ morphology awardees, discuss Gary's poster during the Poster Session. Dr. Dreyfus currently serves on the Foundation's Pharmacology/ Morphology Advisory Committee.

Those who concluded their awards in 1992 are:

James J. Galligan, Ph.D, Assistant Professor, Department of Pharmacology and Toxicology, Michigan State University.

Anna T. Riegel, Ph.D., Assistant Professor, Department of Pharmacology, Georgetown University, School of Medicine.

Philip C. Smith, Ph.D., Assistant Professor of Pharmacy, College of Pharmacy, University of Texas at Austin. Dr. Smith transferred his award in July 1992 to the University of North Carolina, Chapel Hill.

Fellowships for Advanced Predoctoral Training in Pharmacology or Toxicology

Progress in pharmacological research requires the constant entry of well-trained investigators into the field. This program is designed to assist 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. In 1993, the Basic Pharmacology Advisory Committee recommended that the number of awards for this program be increased from ten awards to 13. The Board of Directors approved this recommendation for 1994. The program, in its 16th year, has awarded a total of 195 fellowships.

Those who have been awarded 1993 fellowships beginning between January and July are:

Susan M. Cohen, Duke University, School of Medicine: "The Role of Proline in Synaptic Transmission of the Hippocampal Formation." Ms. Cohen's advisor is J. Victor Nadler, Ph.D., Professor of Pharmacology.

Henry M. Colecraft, University of Rochester, School of Medicine and Dentistry: "Muscarinic Receptor Mediated Stimulation of the Heartbeat in Cultured Heart Cells." Mr. Colecraft's advisor is Dr. Shey-Shing Sheu, Associate Professor, Department of Pharmacology.

Bevin Page Engelward, Harvard School of Public Health: "Characterization of a Mouse DNA Alkylation Repair Gene." Ms. Engelward's advisor is Dr. Leona D. Samson, Associate Professor of Molecular and Cellular Toxicology.

PMA Foundation Scientific Advisory Committee Chairman Frederick M. Radzialowski, Ph.D., makes a point during dinner with FDA's Carl C. Peck, M.D.

Guoping Feng, State University of New York at Buffalo, School of Medicine and Biomedical Sciences: "Molecular and Cytogenetic Analysis of a Mutation Which Affects Sodium Channel." Ms. Feng's advisor is Linda M. Hall, Ph.D., Professor of Biochemical Pharmacology.

Michael S. Grotewiel, Vanderbilt University, School of Medicine: "The Role of G Protein Coupling in $5HT_2$ Receptor Regulation by Agonists and Antagonists." Mr. Grotewiel's principal thesis Advisor is Dr. Elaine Sanders-Bush, Professor of Pharmacology.

Clarissa J. Haugsness, University of Kansas Medical Center, School of Medicine: "Modulation of Renal Cystic Epithelial Cell Differentiation in Polycystic Kidney Disease." Ms. Haugsness' thesis advisor is Jared J. Grantham, M.D., Professor of Medicine.

Saraswati R. Kenkare, University of California, San Francisco, School of Pharmacy: "Nitroglycerin Metabolism and Correlation to Its Biochemical Response and Pharmacologic Effects." Ms. Kenkare's principal advisor is Dr. Leslie Z. Benet, Professor and Chair.

Sheryl Ames Mason, University of South Carolina, School of Medicine: "The Role of Receptor Phosphorylation in Glucocorticoid Hormone Action." Ms. Mason's thesis advisor is Dr. Paul R. Housley, Assistant Professor of Pharmacology.

James M. Rusnak, University of Pittsburgh, School of Medicine: "Intracellular Signalling Pathways in the Programmed Cell Death of Androgen-Independent Human Prostatic Carcinoma Cells." Mr. Rusnak's fellowship advisor is Dr. John S. Lazo, Professor and Chairman of Pharmacology.

W. Bruce Sneddon, Dartmouth Medical School (one year): "Study of the Expression of Parathyroid Hormone (PTH) Receptors in Kidney." Mr. Sneddon's thesis advisor is P. A. Friedman, Ph.D., Professor of Pharmacology.

Elizabeth A. Thomas, University of California, Irvine, College of Medicine (one year): "A Physiological Role for the M2 Muscarinic Receptor in Smooth Muscle." Ms. Thomas' thesis advisor is Dr. Frederick J. Ehlert.

Those who received fellowships in 1992 and continued in 1993 are:

Janet E. Clark, Yale University School of Medicine.

Cathleen Peterson Duncan, Duke University School of Medicine.

Dawn Louise Duval, University of Nevada School of Medicine.

Bonnie Lynne Firestein, University of California, San Diego.

Annette Elizabeth Fleckenstein, Michigan State University.

Tanmoy C. Ganguly, University of Kentucky School of Medicine.

Richard D. Griner, Jr., University of Georgia, College of Veterinary Medicine.

Diane F. Kelly, University of Massachusetts Medical Center.

Margy S. Lambert, University of California, Berkeley.

Suk-Kyeong Lee, Northwestern University Medical School.

Elizabeth A. O'Donnell, University of Pennsylvania.

Leonidas Tsiokas, New Jersey Medical School, University of Medicine and Dentistry of New Jersey.

John Stephen Verbanac, Wayne State University College of Pharmacy and Allied Health Professions.

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, 89 awards have been made to date.

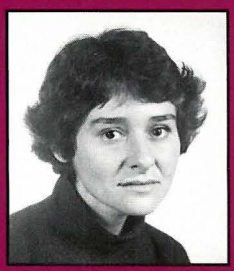
In order to be eligible for an award, the candidate must possess formal training in a morphologic specialty or in pharmacology. However, subsequent training in the complementary discipline, during the period of the fellowship, may be informal. On completion of the program, the fellow should be able to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

Recipients of the fellowship beginning July 1993 are:

Holly Boettger-Tong, Ph.D.

Holly Boettger-Tong, Ph.D., University of Texas Medical School: "Blockade of Estrogen Induce Uterine Proliferation by Retinoids." Estrogen replacement therapy has been used for many years to prevent osteoporosis and relieve vasomotor symptoms in postmenopausal women, and more recently to prevent the increased incidence of cardiovascular disease that occurs after menopause. The efficacy of estrogens for this purpose is well substantiated, but epidemiological studies have conclusively established that unopposed estrogen increases the risk of endometrial carcinoma. This led to the use of estrogens combined with a progestin to decrease the incidence of endometrial cancer. Unfortunately, it is now recognized that progestins may increase the risk of breast cancer and cardiovascular disease. Thus, there is a need to develop new pharmacological approaches that will block the increase in endometrial carcinoma that results from unopposed estrogen without increasing the risk of breast cancer or cardiovascular disease associated with progestins. Retinoic acid has recently been found to limit the proliferation of epithelial cells in many systems and is currently used to treat several types of cancer. Therefore, Dr. Boettger-Tong's research involves testing the hypothesis that retinoids might be used pharmacologically to decrease the uterine growth response to estrogens. She will use a combination of molecular pharmacology and cell biology approaches to prove or disprove this hypothesis.

Galina Kuznetsov, Ph.D., Dana-Farber Cancer Institute, Harvard University: "Function of Tensin as a Tumor Suppressor Component of Adherens Junctions." Tensin is a tyrosine-phosphorylated 200 kDa component of adherens junctions of a variety of cell types, including avian, rodent, and human cells. Previous work in the laboratory of Dr. L. B. Chen has provided initial experimental evidence that tensin may couple cytoskeleton to signal transduction pathways involved in the action of mitogenic growth factors and tumor promoters. The objective of the proposed research is: (1) to create an experimental system for investigation of the potential role of tensin as a signal-transducing protein component of adherens junctions; (2) to use this system to investigate the potential role of tensin in modulating actions of growth factors and tumor promoters on cell morphology and proliferation; and (3) to study the role of tensin in morphological and biochemical changes associated with oncogenic transformation.



Galina Kuznetsov, Ph.D.

Song Song, M.D., Harvard University Medical School: "Gene Therapy for Parkinson's Disease with HSV-1 Vector System." Current therapies for Parkinson's Disease, oral administration of L-Dopa or grafting of dopamine producing cells into the corpus striatum focus on elevating striatal dopamine levels, and are effective initially, but gradually loose their efficacy. A gene therapy approach to Parkinson's Disease with great potential is to introduce the dopamine biosynthetic machinery directly into striatal cells using a defective Herpes Simplex virus (HSV-1) Vector system developed in Dr. Song's laboratory. Using the rat model of Parkinson's Disease, they have demonstrated that expression of tyrosine hydroxylase in striatal cells causes significant (approximately 70%) behavioral recovery for at least one half year. To evaluate the potential of this approach, Dr. Song's experiments propose to determine the efficacy of long-term (one year) behavioral recovery, and to optimize behavioral recovery by directly efficient synthesis of dopamine to the optimum cell type.

Song Song, M.D.

Individuals who began their awards in July 1992 are:

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

David A. Jones, Ph.D., University of Utah School of Medicine.

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

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

Those entering the second year of their fellowship in 1992 are:

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

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.

Ending their awards in 1992 are:

Andrew Bean, Ph.D., Departments of Histology and Neurobiology, Karolinska Institute.

Ellen B. Cornbrooks, Ph.D., Department of Anatomy and Neurobiology, College of Medicine, University of Vermont.

Kathleen Gogas, Ph.D., Harvard University (transferred her award from University of California, San Francisco, in 1992).

Cynthia J. Ziegra, V.M.D., Ph.D., Cornell University College of Veterinary Medicine (ended award June 1993 to take position with Springborn Laboratories in Spencerville, Ohio).

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. As indicated last year, with the concurrence of the Board, the Scientific Advisory Committee has decided to phase out this program after 1992 due to 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 at which time this program offered $30,000 per year for two years' salary and fringe benefits. The total number of awards made for this program is 18.

Entering her second year in 1993:

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."

Ending their awards in 1993:

Renate Reimschuessel, V.M.D., Ph.D., Assistant Professor, Department of Pathology, School of Medicine, University of Maryland.

Thomas J. Rosol, Assistant Professor, Department of Veterinary Pathobiology, The Ohio State University.

Pharmaceutics

Undergraduate Research Fellowships in Pharmaceutics

This fellowship program began in 1990 and is designed to offer support to undergraduate students in pharmaceutics to give the student an opportunity to participate in a meaningful research project with a motivated, inspiring and research-active pharmaceutics faculty member. It provides a selected pharmaceutics faculty member with a one-year fellowship for $5,000 which the faculty member can provide to a qualified undergraduate of their choosing. Twelve awards are budgeted for this award. Including those awards for 1993, this program has assisted 47 undergraduate students.

Faculty and their undergraduate students who will receive fellowships between January and August 1993 are:

Jane P. F. Bai, Ph.D., Assistant Professor, Pharmaceutics Department, University of Minnesota, College of Pharmacy. **Student: Uyen Nhu Tang—**"Insulin Metabolism by Intestinal Mucosal Cell Proteolytic Activities."

Jane P. F. Bai, Ph.D., Assistant Professor, Pharmaceutics Department University of Minnesota, College of Pharmacy. **Student: Thomas Trinh—**"The Longitudinal Distribution of Lysosomal Proteases Along the Rat Intestine."

Physical State and Release Characteristics of Drugs in Microcapsule Formulations."

James N. Herron, Ph.D., Assistant Professor, University of Utah, College of Pharmacy.
Student: Sean Davies—"Development of a PEG-Coated Immunoliposome."

Vincent H.L. Lee, Ph.D., Assistant Professor, University of Southern California, School of Pharmacy.
Student: Benjamin J. Schatzman—"Oligonucleotide Transport Across Cultured Tracheal Epithelium of the Rabbit."

Duane E. Ruffner, Ph.D., Assistant Professor, University of Utah College of Pharmacy.
Student: Robynne W. Kirkpatrick—"Polycations as Carriers for Efficient Uptake of Antisense Oligonucleotides."

Teruna J. Siahaan, Ph.D., Assistant Professor, University of Kansas, School of Pharmacy.
Student: Matthew W. Conrad—"Conformational Study of Calcium Binding Peptide from E-Cadherin."

Philip C. Smith, Ph.D., Assistant Professor, University of North Carolina at Chapel Hill, School of Pharmacy.
Student: James Daniel Whisnant III—"Toxicokinetics of Salicyl Acyl Glucuronide: Disposition and Covalent Binding to Proteins *In Vivo*."

Samuel H. Yalkowsky, Ph.D., Professor of Pharmaceutics, University of Arizona, College of Pharmacy.
Student: Christopher Sullivan—"Cosolvent Induced Hemolysis."

Alekha K. Dash, Ph.D., Assistant Professor, Creighton University, School of Pharmacy and Allied Health Professions.
Student: Steve D. Junker—"Effects of Lyophilization on the

Pausing during the reception are (l to r) Foundation President Bectel, Terrance Blaschke, M.D., a former faculty awardee and current member of the Clinical Pharmacology Advisory Committee, and CDER Director Carl C. Peck, M.D.

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 and $500 a year for incidentals directly associated with the preparation of the dissertation. The program provides seven, two-year fellowships annually. Because of additional monies returned to the program, nine awards were made for 1993 bringing the total number of awards to 40.

Those who received fellowships beginning between January and July 1993 are:

Kim Hancock, Purdue University, School of Pharmacy–"Understanding and Controlling Surface Area Changes During the Aging of Amorphous Powders. Ms. Hancock's thesis advisor is Dr. Dane Kildsig, Professor of Physical Pharmacy.

Huai-Hung Danny Kao, University of Kentucky, College of Pharmacy–"Enhancement of Delivery of L-Dopa by the Administration of its Prodrugs via the Nasal Route." Mr. Kao's principal advisor is Dr. Anwar Hussain, Professor of Pharmacy, Medicinal Chemistry and Pharmaceutics.

Sandy Koppenol, University of Wisconsin-Madison, School of Pharmacy–"Molecular Mechanisms of Lipid Bilayer Fusion Induced by Calcium and Calcium-Dependent Phospholipid-Binding Proteins." Ms. Koppenol's fellowship advisor is Dr. George Zografi, Professor of Pharmacy.

Gil Mannering, Ph.D., member of the Clinical Pharmacology Advisory Committee, and Britta Mattson, Ph.D., former awardee and currently with Merck, Sharpe & Dohme, discuss the morning's activities at the Annual Awardee Meeting general session

Jason LePree, University of Wisconsin-Madison, School of Pharmacy—"Solvent Effects on Chemical Reaction Rates." Mr. LePree's thesis advisor is Dr. Kenneth A. Connors, Professor of Pharmaceutics and Acting Dean.

Jeffrey David Lewis, Purdue University, School of Pharmacy and Pharmacal Sciences—"Aggregation of Immunoglobulin During Purification by Affinity Chromatography." Mr. Lewis' fellowship advisor is Dr. Dane O. Kildsig, Department Head, Professor of Physical Pharmacy.

Carlos Noel Velez, University of North Carolina at Chapel Hill, School of Pharmacy-"Antigen Delivery to M Cells of Peyer's Patches by Means of Sensitized Liposomes for Stimulation of Mucosal Immunity." Mr. Velez's thesis advisor is Moo J. Cho, Ph.D., Associate Professor of Pharmaceutics.

Wan-Ching Yen, University of Southern California, School of Pharmacy—"Peracellular Peptide Transport Across the Rabbit Intestine." Mr. Yen's principal advisor is Vincent H. L. Lee, Ph.D., Professor and Chairman, Department of Pharmaceutical Sciences.

Those who received fellowships in 1992 and continued 1993 are:

Shyue-Fang Hsu, Department of Pharmaceutics, University of Wisconsin-Madison School of Pharmacy.

Michelle T. Marra, Department of Pharmaceutics, University of Utah College of Pharmacy.

Paul B. Myrdal, Department of Pharmaceutics, University of Arizona College of Pharmacy.

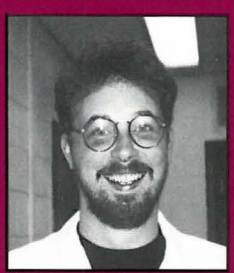
Robert G. Strickley, Department of Pharmaceutics, University of Utah College of Pharmacy.

Postdoctoral Research Fellowships in Pharmaceutics

Complementing the other two pharmaceutics programs offered by the PMA Foundation, the Postdoctoral Research Fellowships in Pharmaceutics entered its second year of existence. 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 PMA 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 award per year.

In 1993, the following individuals received awards:

Jeffrey A. Hughes, Ph.D., University of North Carolina at Chapel Hill School of Medicine—"The Effect of Physiochemical Properties of Antisense Oligonucleotides on Their Membrane Penetration Characteristics." The major advantage of oligonucleotides is the specificity that the Watson-Crick interactions offer these molecules. This interaction can stop the expression of specific genes by interfering with transcription, message processing, RNA stability or translation. Two limitations which are associated with oligonucleotides as drugs are their rapid degradation in the body and their poor cellular permeability. The degradation problem has been addressed by the synthesis of chemically modified compounds which offer some degree of resistance to metabolic processes. The issue of cellular permeability of these large polar compounds are starting to be addressed in literature. To be able to synthesize new oligonucleotides which will have better cellular permeation, a better understanding of cellular transport mechanisms needs to be gained. It is the purpose of Dr. Hughes' study to look at different physiochemical properties of oligonucleotides which influence their membrane penetration as tested in model liposome formations. By addressing this permeability, mechanisms in a systematic fashion , we should be able to identify structural features which influence membranes permeability. After oligonucleotide candidates are identified which demonstrate good permeability, these candidate will be compared to standard oligonucleotides in tissue culture systems to determine the cellular mechanisms of uptake and distribution.



Jeffrey A. Hughes, Ph.D.

Lawrence Ka-Yun Ng, Ph.D.

Lawrence Ka-Yun Ng, Ph.D., University of Kansas, School of Pharmacy—"Encapsulation of a Chemical Mediator, Histamine, in Target-Sensitive Immunoliposomes to Improve the CNS Delivery of Non-lipophilic Compounds." Dr. Ng's research will attempt to improve the CNS delivery of polar drug molecules by transiently increasing the permeability of the blood-brain barrier (BBB) at the time of delivery. This will be accomplished by the targeted delivery of polar drug molecules and histamine to the BBB using target-sensitive immunoliposomes which destabilize and release their contents upon binding to their specific receptors on brain endothelium. Upon its release, histamine will cause endothelial cells to contract and create temporary intercellular gaps between endothelial cells, thus allowing polar drug molecules to enter the brain. To determine the feasibility of this approach, the following studies will be carried out to ascertain that: (a) histamine will generate the same endothelial cell contraction effect on brain endothelium: (b) conjugation of anti-transferring receptor antibody OX-binding of the immunoliposomes to transferring receptors on brain endothelium will result in destablization of immunoliposomes and the release of their contents; and (d) site-specific release of histamine and polar drug molecules from immunoliposomes will contribute to the increase in the BBB permeability of polar drug molecules *in vitro* and *in vivo*.

Beginning their awards in 1992:

Prashant J. Chikhale, Ph.D., University of Kansas, School of Pharmacy—"A Redox-Sensitive Prodrug Approach Toward Optimizing Delivery of Acivicin to Solid Tumors and Minimizing its Toxicity to the Central Nervous System."

Michael Mulski, Department of Chemical Engineering and Materials Sciences, University of Minnesota, "Water Vapour Transport in Semi-Crystalline Polymer Films—A Model Based on Percolation Theory."

Raymond D. Skwierczynski, University of Wisconsin-Madison, Medical School—"The Influence of Nonhydrogen-Bonded Bipole-Dipole Interactions on the Solid-State Organization of Organic Molecules."

Research Grants

An important aspect of the PMA 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 PMA 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 allows for approximately 16 research starter grants each year at $12,500 per year with the second year contingent upon need. The first awards were made in 1972, and a total of 460 research starter grants have been made, including the 20 awards beginning January 1, 1993.

Recipients of the grants beginning January 1993 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

Timothy John Connelly, M.D.
University of Wisconsin-Madison
Medical School

Terrance M. Egan, Ph.D.
Saint Louis University
School of Medicine

Miriam Falzon, Ph.D.
University of Texas
Medical School at Galveston

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.
Thomas Jefferson University
Jefferson Medical College

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

Patson T. Nhamburo, Ph.D.
University of Maryland
School of Medicine

Edwards A. Park, Ph.D.
University of Tennessee, Memphis
College of Medicine

Stuart W. Peltz, Ph.D.
University of Medicine and Dentistry of New Jersey
Robert Wood Johnson Medical School

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

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

Teruna J. Siahaan, Ph.D.
University of Kansas
School of Pharmacy

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

Andrea J. Yool, Ph.D.
University of Arizona
College of Medicine

Based on need for funds, a review of the 17 research starter grantees whose awards began January 1, 1992, for a second year of the awards resulted in nine of them having their awards continued. These are:

Michael Babich, Ph.D.
University of Illinois
College of Medicine

Jane P. F. Bai, Ph.D.
University of Minnesota
College of Pharmacy

James K. Bashkin, Ph.D.
Washington University
Graduate School of Arts & Sciences

A. Leslie Morrow, Ph.D.
University of North Carolina at Chapel Hill
School of Medicine

Sunday Edet Ohia, Ph.D.
Creighton University
School of Pharmacy

Mary Beth St. Clair, Ph.D.
North Carolina State University

Roseann L. Vorce, Ph.D.
University of Nebraska
Medical Center

Donald E. Walters, Ph.D.
Auburn University
School of Pharmacy

William Frederick Wonderlin, Ph.D.
West Virginia University
Health Sciences Center

Foundation Scientific Consultant Edward J. Cafruny, M.D., Ph.D., shares a laugh with Felix A. de la Iglesia, M.D., as he presents a plaque of recognition for the work of the Toxicologic-Pathology Advisory Committee and its chairman, Dr. James Newberne.

Purpose

The PMA 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.

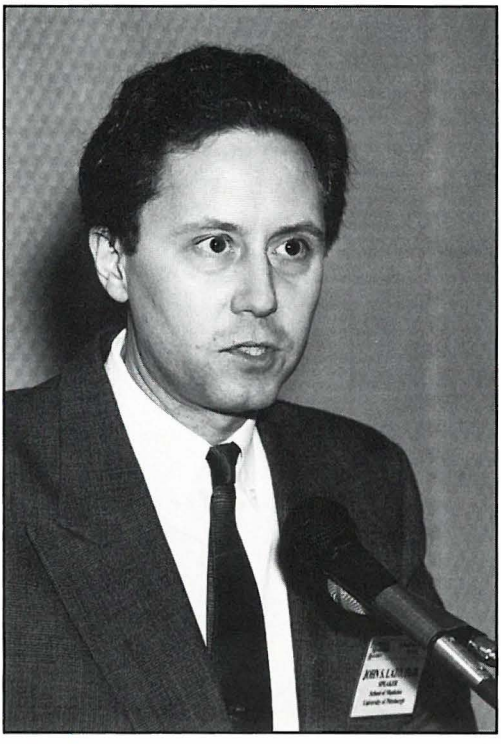
(2) Funds for construction. The Foundation is not unmindful of the needs and the tremendous pressures for private funds for construction projects. However, it is believed that the scientific community can be better served by channeling the Foundation's available resources into other areas.

(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 33 and under the Education and Training Programs Section on page 12.

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



Speaking on "Anticancer Drug Resistance" at the Awardees Meeting is John S. Lazo, Ph.D., of the University of Pittsburgh School of Medicine.

Report of the Treasurer

Robert C. Black
Secretary-Treasurer
PMA Foundation

Since its inception in 1965, the PMA Foundation has been supported by the generosity of the research-intensive pharmaceutical manufacturers–the PMA member firms, associates and research affiliates. The total income of the Foundation in 1992 was $2,589,242. Of this amount, $2,363,850 came from contributions. The balance of $225,392 came from investments and refunds of unexpended balances from grants.

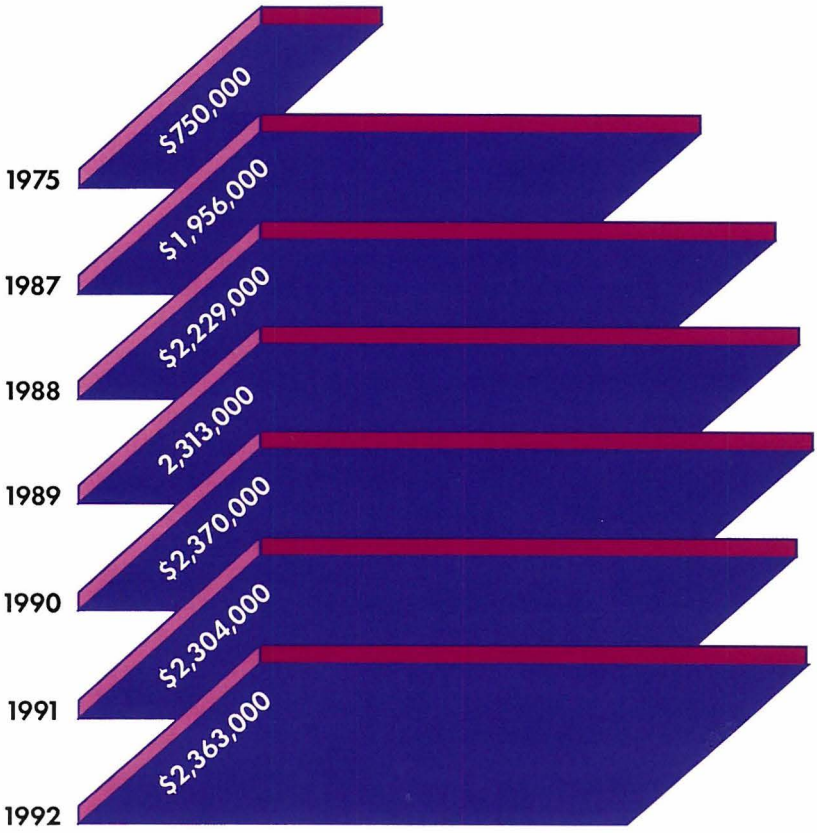
In 1992, grants totaled $1,899,246; Foundation Annual Awardee Meeting and ASPET meeting amounted to $87,421; Honoraria and Professional Services totaled $92,023, Committee Meetings amounted to $89,262; special meetings and other expenses for 1992 amounted to $424,343. The total fund balance as of December 31, 1992, was $5,288,186. 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, 1992, the contingency liability for 1993-96 was approximately $3,422,465.

The Foundation's financial position as of December 31, 1992, has been audited by the Washington D.C. accounting firm of Buchanan & Company.

Robert C. Black
Secretary-Treasurer
PMA Foundation
and
President
ZENECA Pharmaceuticals Group

PMA Foundation Income

1975 - 1991 (thousands)



Statement of Income and Expenditures For the Year Ended December 31, 1992

Income	
Contributions	2,363,850
Interest from investments	93,811
Interest Transferred from Future Commitment Fund	101,000
Miscellaneous Income	30,581
Total Income	**2,589,242**
Expenditures	
Grants–Note A	
Clinical Pharmacology Unit Award	102,257
Faculty Awards in Clinical Pharmacology	400,000
Faculty Awards in Basic Pharmacology	180,000
Fellowships for Careers in Clinical Pharmacology	85,000
Advanced Predoctoral Fellowships in Pharm/Tox	310,500
Pharmacology-Morphology Fellowships	188,656
Medical Student Research Fellowships	55,833
Research Starter Grants	270,000
Faculty Awards in Toxicologic-Pathology	105,000
Advanced Predoctoral Fellowships in Pharmaceutics	99,500
Undergraduate Fellowships in Pharmaceutics	65,000
Postdoctoral Fellowships in Pharmaceutics	37,500
Grant Total	1,899,246
Administrative	
February Awardee Meeting and Annual ASPET Meeting	87,421
Committee Meetings and Travel	89,262
Special Projects	53,741
Honoraria and Professional Services	92,023
Publications	68,289
Office Expense	56,216
Rent, Salaries, Taxes	246,097
Administrative Total	693,049
Total Expenditures	**2,592,295**
Excess of income over expenditures	(3,053)
Operating fund balance at January 1, 1992	2,943,434
Operating fund balance December 31, 1992	3,041,381
Future Commitment Fund (Reserve Fund) (Note B)	2,080,188
Total fund balance at December 31, 1992	**5,121,569**

Note A – In addition to the amounts shown, the Foundation is committed, subject to annual review, to make certain grants. At December 31, 1992, the amounts still to be disbursed with respect to these grants amounted to aggregated $3,422,465 with $1,890,202 of this to be disbursed during 1993; $1,173,523 in 1994; $298,740 in 1995; and $60,000 in 1996.

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

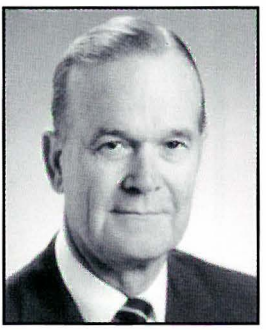
Income from Investments	117,249
Interest Transferred to Operating Fund	(101,000)
Dividend Income	3,918
Gain (Loss) on Sale of Stock	22,815
Less: Trust Commission Expense	(11,131)
Excess of expenditures over income:	**31,851**
Future Commitment Fund Balance at January 1, 1992	2,149,337
Future Commitment Fund Balance at December 31, 1992	**2,080,188**

Organization and Administration

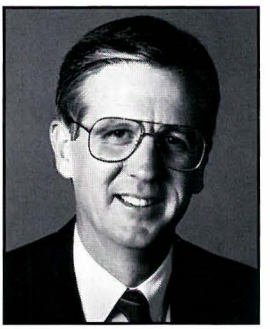
The PMA Foundation operates through its officers, Board of Directors and five advisory committees. In March of 1993, Charles A. Sanders, M.D., Chairman and Chief Executive Officer of Glaxo Inc., was re-elected Chairman. Although Theodore Cooper, M.D., Ph.D., Chairman and Chief Executive Officer of The Upjohn Company, was re-elected Vice-Chairman, due to Dr. Cooper's death in April, Mr. Phillip R. Tracy, President and Chief Executive Officer, Burroughs Wellcome Co., was elected to fill his unexpired term. Mr. Robert C. Black, President of ZENECA Pharmaceuticals Group, was elected Secretary-Treasurer.

Maurice Q. Bectel, D.Sc., again served as the Foundation's President. During the year, Donna Moore was promoted to the new position of Director of Programs. Edward J. Cafruny, M.D., Ph.D., and C. Joseph Stetler, Esq., continue to serve as Foundation consultants—Dr. Cafruny as scientific consultant and Mr. Stetler as staff counsel.

1993 Officers



Charles A. Sanders, M.D.
Chairman
PMA Foundation
Chairman and Chief
Executive Officer
Glaxo Inc.
Research Triangle Park,
North Carolina



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

Robert C. Black
Secretary-Treasurer
PMA Foundation
President
ZENECA Pharmaceuticals
Group
Wilmington, Delaware

Maurice Q. Bectel, D.Sc.
President
PMA Foundation

* Mr. Phillip Tracy will fill the unexpired term of Dr. Theodore Cooper as Vice Chairman of the Board.

1993 Board of Directors

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Pharmaceuticals
Procter & Gamble USA
The Procter & Gamble
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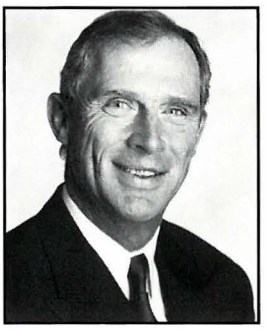
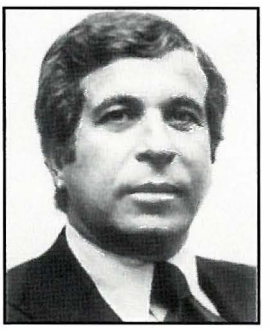
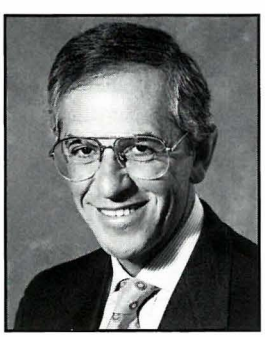
Cincinnati, Ohio



Jan Leschly
Chairman
SmithKline Beecham
Pharmaceuticals
Philadelphia, Pennsylvania



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



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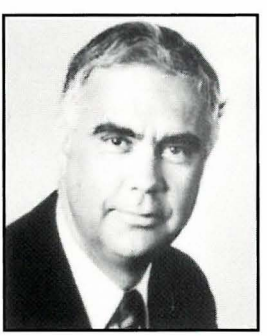
Indianapolis, Indiana



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Johnson & Johnson
New Brunswick, New Jersey

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President
Pharmaceutical
Manufacturers
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Washington, D. C.
(Ex-Officio)

*Joined the Board in March 1993

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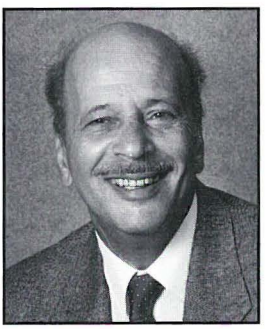
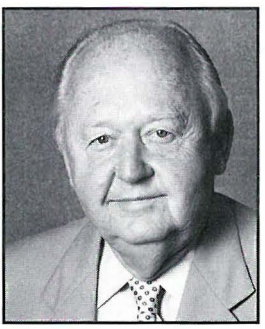


Edward J. Cafruny, M.D., Ph.D.
Emeritus Distinguished University Professor
University of Medicine and Dentistry of New Jersey



C. Joseph Stetler, Esq.
Attorney at Law

Donna Moore
Director of Programs

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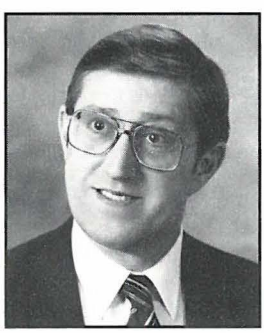
Scientific Advisory Committee



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Chairman and Professor
Department of Medicine
Brown University
Providence, Rhode Island

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Professor and Chairman
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Columbia University
College of Physicians and Surgeons
New York, New York

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and
Vice Chairman of the Board
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Health Science Center
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Kenilworth, New Jersey

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University of Medicine & Dentistry of New Jersey
Robert Wood Johnson Medical School
Piscataway, New Jersey

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Consultant
Searle
Skokie, Illinois

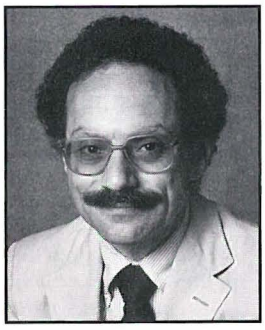
** Joined the Committee in May 1993*

Frank G. Standaert, M.D.
Perrysburg, Ohio

***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



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Professor and Former Chairman
Department of Pharmacology
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Dean, School of Veterinary
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West Lafayette, Indiana

* Joined the Committee in July 1993

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Duke University Medical Center
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University of California,
San Francisco
San Francisco, California

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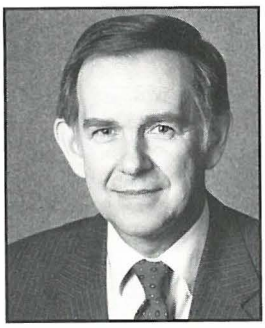
and
Executive Vice President and
Chief Academic Officer
Medical College of Pennsylvania
Philadelphia, Pennsylvania

Pharmaceutics Advisory Committee



James Swarbrick, D.Sc., Ph.D.
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College of Pharmacy
University of Utah
Salt Lake City, Utah

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Vice President
Pharmaceutical Development
Glaxo Inc.
Research Triangle Park, North
Carolina

Anthony A. Sinkula, Ph.D.
Kalamazoo, Michigan

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

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Applications

Descriptive brochures and application forms for all of the PMA Foundation Grant Programs listed on the back inside 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 Manufacturers Association Foundation, Inc.
1100 Fifteenth Street, N. W.
Washington, D.C. 20005
(202) 835-3470
(202) 467-4823 (fax)

PMA Foundation Current Programs for 1994

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)	4 budgeted/ 2 years	$ 192,000 total $ 24,000 per award per year	October 1 December 15 July 1
(3) Medical Student Research Fellowships (1974-Amended 1982)	8 budgeted/ 3 months to 24 months	$ 80,000 total $ 833 per month maximum $ 10,000	January 15 March 15 July 1
(4) Development Grants for Clinical Pharmacology Units (1978)	1 budgeted/ 3 years to use funds	$ 100,000 per award	January 15 March 15 July 1
Basic Pharmacology Advisory Committee			
(5) Faculty Awards in Basic Pharmacology/Toxicology (1973)	3 budgeted/ 2 years	$ 180,000 total $ 30,000 per award per year	September 15 December 15 July 1
(6) Research Starter Grants (1972)	16 budgeted/ 2 years	$ 400,000 total $ 12,500 per award per year	September 1 December 15 January 1
(7) Advanced Predoctoral Fellowships in Pharmacology/Toxicology (1978)	13 budgeted/ 1 or 2 years	$ 325,000 total $ 12,500 per award per year	September 15 December 15 January-August
Pharmacology-Morphology Advisory Committee			
(8) Fellowships in Pharmacology-Morphology including Cell Biology (1968)	4 budgeted/ 2 years	$ 172,000 total $ 21,500 per award per year	January 15 March 15 July 1
Pharmaceutics Advisory Committee			
(9) Advanced Predoctoral Fellowships in Pharmaceutics (1987)	7 budgeted/ 1 or 2 years	$ 175,000 total $ 12,500 per award per year	October 1 December 15 January-August
(10) Undergraduate Research Fellowships in Pharmaceutics (1990)	12 budgeted/ 1 year	$ 60,000 total $ 5,000 per award	October 1 December 15 January-July
(11) Postdoctoral Fellowships in Pharmaceutics (1992)	2 budgeted/ 1 or 2 years	$ 100,000 total $ 25,000 per award per year	October 1 December 15 January-December

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

Pharmaceutical Manufacturers Association Foundation
1100 Fifteenth Street, N.W.
Washington, D.C. 20005